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MISCELLANEOUS ARTICLES

FORMATION

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Original Contributions

Pathogenesis of Acute Pancreatitis

ARCHIE H. BAGGENSTOSS, M.D.
Rochester, Minnesota

PRESENT knowledge regarding the pathogenesis of acute pancreatitis has been derived from clinical and pathologic observations of patients and from experimental methods. It is not worth while, nor is it my purpose, to extol the virtues of one over the other. Each method has its own advantages and disadvantages. Clinical and pathologic observation of nature's experiments can always be criticized because of the lack of controls. Experimental investigation, on the other hand, is hampered because may of the sequences observed in human beings cannot be duplicated in the laboratory. Both types of investigation are necessary if a thorough understanding of this mysterious disease is to be gained. Nothing is better for the experimentalist than a broad experience in the clinical and pathologic manifestations of pancreatitis, and for the clinician or pathologist nothing is better than the use of controlled experiments to broaden concepts and stimulate imagination.

Experimental Pancreatitis

Acute pancreatitis has been produced experimentally by a wide variety of methods. Among the methods used are the injection of bile,[1] trypsin[2] and other substances[3] into the pancreatic ducts; blockage of the ducts associated with stimulation of pancreatic secretion;[3-5] obstruction of ducts with stimulation of secretion and interference with blood supply;[6] use of high-fat, low protein diets;[7,8] administration of ethionine[9,10] or mecholyl;[11] stimulation of the left splanchnic nerve;[12] and administration of large doses of cortisone.[13]

Thal and Brackney[14] have been able to produce fulminating hemorrhagic pancreatitis in rabbits and goats by introducing meningococcic or Escherichia coli endotoxin into the pancreatic duct at pressures well below those required to produce ductal rupture and, subsequently, inducing the Shwartzman phenomenon by intravenous injection of the same toxin. In control experiments in which the intravenously administered provocative dose was omitted, pancreatic necrosis failed to occur in all cases. Histologic studies uniformly showed capillary and venular hyalin thrombosis. These ingenious experiments refocus attention on the importance of infection in pancreatitis and will be referred to later.

A few years ago Block, Wakim and I[15] wished to re-examine certain factors which are involved in the experimental production of pancreatitis. We were particularly concerned whether a common channel between the common bile and pancreatic ducts is important in the pathogenesis of acute pancreatitis and whether in certain cases acute pancreatitis might not be solely the result of interference with blood supply. We used the rat for these studies for two reasons:

1. Anatomically the external secretion of the pancreas enters into the common duct by way of many small ducts, thus permitting study of the theory of the common channel as an etiologic factor.

2. The changes in the pancreas of the rat after occlusion of the pancreatic duct appeared to be more extensive than in other species, as, for example, the dog.

By occluding the common bile duct at the duodenum it was possible to produce a common channel. By ligating at the hilus of the liver, bile

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Read at the Continuation Course on Emergency Surgery for General Physicians at the University of Minnesota, Minneapolis, Minnesota, January 30 to February 1, 1958.

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The Mayo Foundation, Rochester, Minnesota, is a part of the Graduate School of the University of Minnesota.

could be excluded from the common duct and ligation at the duodenum would test the effect of obstruction without a common channel. The

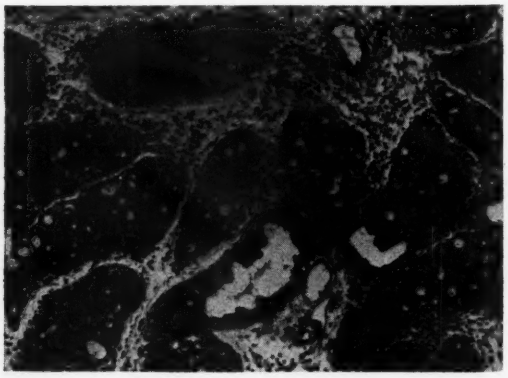

Fig. 1. Acute interstitial pancreatitis in the rat (partial obstruction of ducts). Note dilatation of ducts (hematoxylin and eosin; reduced from x100).

effects of both partial and complete occlusion also were examined. Different degrees of ischemia of the pancreas were produced by varying the extent of reduction of circulation.

In general, whenever obstruction to the flow of pancreatic juice was produced, the gross changes consisted of pancreatic edema and varying degrees of fat necrosis in the region of the pancreas and throughout the abdomen. Histologic examination of the pancreas disclosed dilatation of ducts and acini; edema with infiltration, predominantly interlobular, of lymphocytes, monocytes, and a few polymorphonuclear leukocytes; atrophy and degenerative changes of the acini; and necrosis of intrapancreatic and extra-pancreatic fat. Pancreatic parenchymal necrosis and hemorrhage, however, occurred infrequently. It was found that the changes were the same whether or not a common channel existed and whether obstruction was complete or partial (Fig. 1).

Occlusion of pancreaticoduodenal arteries alone without interference with the flow of the external secretion produced only a slight effect. Occasional foci of parenchymal necrosis with the infiltration of a few lymphocytes, monocytes and segmented leukocytes were observed, but otherwise the pancreas appeared normal. More extensive devascularization of the pancreas by occlusion of more of its arterial supply, however, resulted in marked changes, including necrosis, interlobular and intralobular edema, infiltration of leukocytes, some proliferation of fibroblasts and fat necrosis within the pancreas and to varying

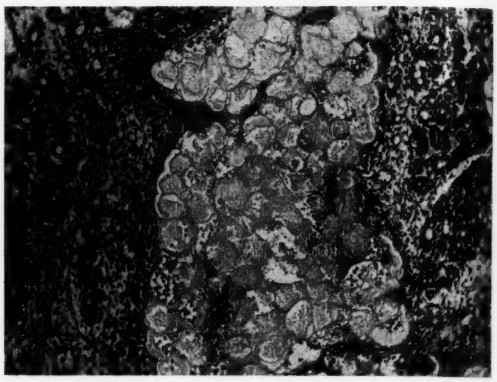

Fig. 2. Acute pancreatic necrosis in the rat produced by obstruction of ducts plus ischemia (hematoxylin and eosin; reduced from x150).

degrees throughout the abdomen. Generally these histologic changes were found in association with local ischemic infarcts.

Inasmuch as pancreatic parenchymal necrosis and hemorrhage were not observed frequently after obstruction to the flow of pancreatic juice alone, varying degrees of temporary and permanent pancreatic ischemia were produced in fifteen animals in addition to ductal obstruction. In these studies pancreatic parenchymal necrosis of varying degrees of severity and extent usually was added to changes previously enumerated as occuring after effective occlusion of the pancreatic ducts (Fig. 2). After ligation of the pancreatiocoduodenal arteries, the areas of necrosis were usually small and scattered; after interference with arterial flow of greater magnitude the areas of necrosis were larger. After temporary occlusion of the arteries for fifteen minutes the necrosis seemed less marked but hemorrhage was severer.

These studies support in general the concepts derived by other investigators concerning the pathogenesis of acute pancreatitis. Acute obstruction of the pancreatic ducts will result in at least one form of acute pancreatitis with peripancreatic fat necrosis, but parenchymal necrosis is generally absent. Degenerative changes and atrophy of acinar cells occur, but parenchymal necrosis usually does not. These changes appear analogous

to those seen in acute edematous or acute interstitial pancreatitis in human beings. The production of a common channel between the bile and pancreatic ducts does not appear to modify the changes significantly.

If ischemia is added to obstruction of the pancreatic duct, parenchymal necrosis is produced in addition to other pancreatic damage. This will vary in severity depending on the degree and extent of arterial occlusion. Hemorrhage accompanies necrosis in some instances, especially if ischemia is temporary. Lesions of this type may be analogous to acute hemorrhagic pancreatitis in human beings.

Complete devascularization of large portions of the pancreas generally resulted in ischemic infarcts, but occasionally acute pancreatitis with pancreatic necrosis and with fat necrosis without dilatation of ducts and acini occurred. Thus a focal form of acute pancreatitis can result from prolonged severe and extensive ischemia alone.

All experimental methods of producing pancreatitis, including ours at the Mayo Clinic, remind me of a statement made by Johannes Müller,[16] a pioneer and leader in physiology, in his inaugural address as professor of physiology at the University of Bonn: "Observation," said he, "is simple, unimpeded, diligent, honest, without prejudiced opinion; the experiment, artificial, impatient, eager, saltatory, passionate, unreliable. Nothing is easier than to perform a number of so-called interesting experiments. It is only necessary to force Nature into a trial and she will always furnish a troubled, passive answer. Noth-

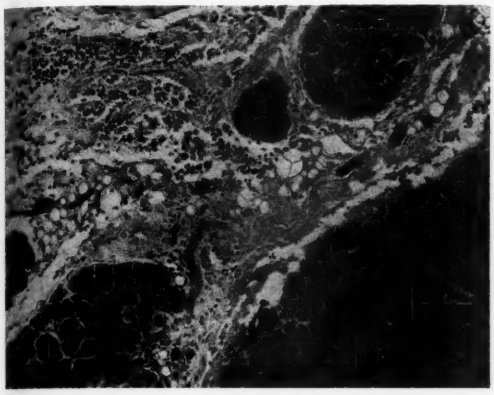

Fig. 3. Acute interstitial pancreatitis in man (hematoxylin and eosin; reduced from x100).

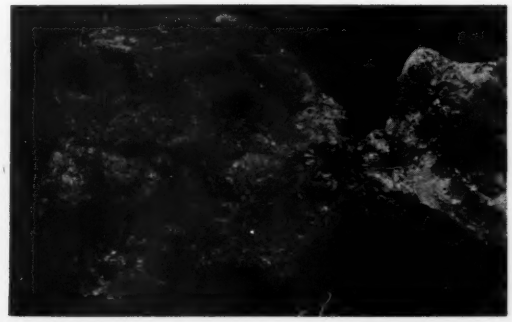

Fig. 4. Acute pancreatic necrosis in man fifty-six years of age. Chronic cholecystitis with stones. One stone in common bile duct at ampulla.

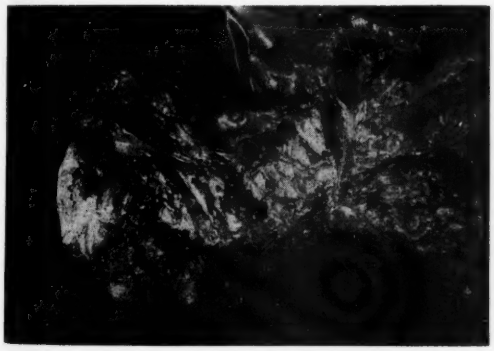

Fig. 5. Acute hemorrhagic pancreatitis in man twenty-nine years of age. No stones in gallbladder or ducts.

Fig. 6. Acute suppurative pancreatitis in woman sixty-one years of age. Note abscess in head. One large stone in gallbladder; no stones or dilatation of bile and pancreatic ducts.

ing is more difficult than to interpret Nature, nothing so difficult as a valid physiological experiment!"

Pathologic Observations

Experimental methods help us to understand acute pancreatitis, but clinical, surgical and pathologic observations regarding this mysterious disease must not be neglected. In fact, it is mandatory that we both plan our experiments and test their validity on the basis of our clinical and pathologic observations if we wish to obtain accurate information on the pathogenesis of acute pancreatitis.

With these thoughts in mind, let us first clarify the condition we are talking about. Pancreatitis is a broad term and embraces a great variety of lesions. Under this heading we may have: (1) acute interstitial pancreatitis (Fig. 3), (2) acute pancreatic necrosis (Fig. 4), (3) acute hemorrhagic pancreatitis (Fig. 5), and (4) acute suppurative pancreatitis (Fig. 6).

Now let us see whether clinical and pathologic observations can teach us anything about the pathogenesis of these conditions.

Acute and Subacute Interstitial Pancreatitis

Evans and associates[17] recently completed a review of all cases of acute and subacute interstitial pancreatitis encountered at necropsy at the clinic. Only twenty-five such cases (0.11 per cent of the necropsies) were found over a period of forty years. Analysis of the clinical histories failed to reveal a uniform specific clinical picture. In fifteen of twenty-five cases abdominal pain during the final illness was not mentioned. In each of the twenty-five cases, acute or subacute interstitial pancreatitis was considered to be an incidental finding at necropsy; in no instance could one be certain that pancreatitis was the dominant factor in the patient's illness or death. Significant findings noted concomitantly with acute and subacute interstitial pancreatitis at necropsy were as follows: diseases of the bile ducts or gall bladder in thirteen cases; evidence of recent intra-abdominal surgical procedures in eight cases; peritonitis, intestinal obstruction, uremia, and hepatitis in three cases each.

Except for the occurrence of intestinal obstruction, uremia and viral hepatitis, the concomitant findings at necropsy in these cases do not differ much from those observed in acute pancreatic necrosis with or without hemorrhage or suppuration. Interesting as they are to the pathologist, however, these cases of acute interstitial pancreatitis, if they do not go beyond this stage, do not as a rule constitute the main concern of the clinician and the surgeon. Whether the condition ever develops into other varieties and how often it does so, are still unanswered questions.

Acute Pancreatic Necrosis

I am mainly concerned in this paper with the other three varieties of pancreatitis, or, as I like to call them, acute pancreatic necrosis with or without hemorrhage or suppuration. In these conditions, as in acute interstitial pancreatitis, disease of the biliary tract seems to be a common accompaniment. In a series of cases studied at necropsy at the Mayo Clinic[18] cholelithiasis was encountered in 78 per cent and stones impacted in the ampulla of Vater in 12 per cent.

Biliary-Tract Disease.—Opie's[19] hypothesis, or the common-channel theory which postulates that a stone impacted in the ampulla of Vater causes pancreatitis, has dominated medical thought for the past half century. According to this theory a gallstone impacted in the ampulla of Vater results in regurgitation of bile into the pancreatic duct and activation of pancreatic enzymes. There are many objections to Opie's[19] theory and these have been reviewed by Ivy and Gibbs[20] and by Richman.[21] Suffice it to say, a common channel frequently is not present and in most patients who have acute pancreatitis and who undergo surgical procedures, it is impossible to demonstrate a stone in the ampulla or in the pancreatic duct.

In every large series of cases of pancreatitis, however, there usually are a few patients, about 5 per cent,[20] who have a common channel obstructed by a stone. In such studies, as in our own, usually a few cases also are found in which stones occur in the common bile duct without the existence of a common channel. In such cases, obstruction of the pancreatic duct may be the important factor. Even if there is no common channel the pancreatic duct may be obstructed by pressure of the stone on the thin septum separating the ducts near the duodenal orifice.[22] Then, of course, acute pancreatic necrosis also has occurred in cases in which there is neither a com-

mon channel nor stones in the duct. In these last-mentioned cases, obstruction of the pancreatic duct may be caused by such conditions as edema of the papilla of Vater or spasm of the sphincter of Oddi. That spasm of the sphincter of Oddi occurs is well known from numerous observations in patients with T tubes in the common bile duct.[23]

Obstruction may occur as a result of pancreatic stones, although this rarely happens, and intrapancreatic obstruction may occur from squamous metaplasia of the ducts. In this connection, it is interesting, however, that we seldom encounter diffuse pancreatic necrosis as a result of complete carcinomatous obstruction of the pancreatic duct. Haunz and I[24] studied twenty-five cases at necropsy in which the main pancreatic duct was completely obstructed by carcinoma and in none of them was diffuse pancreatitis or pancreatic necrosis observed. In 202 cases of carcinoma of the pancreas studied at necropsy[25] only one case of hemorrhagic pancreatitis was encountered.

These facts correlate well with the experimental observations that occlusion of the pancreatic duct alone does not produce pancreatitis but requires the additional factor of secretory stimulation. Clinically, it has long been apparent that the first symptoms of acute pancreatitis often appear after a big meal.

Before leaving the subject of biliary-tract disease, it should be noted that for many years the factor of obstruction has been overemphasized and the factor of infection, underestimated. Thal and Brackney,[14] in this regard, deserve much credit for refocusing our attention on the role of bacterial toxins and the Shwartzman phenomenon in experimental production of the disease. It may therefore be significant that infection of the biliary tract is commonly associated with pancreatitis.[18,26-28] Furthermore, it has been shown repeatedly by cholangiography that regurgitation from ducts and duodenum occurs commonly in the absence of a common channel and regardless of the manner of opening of the ducts.[20,29] Here, then, we have a mechanism of exposing pancreatic ducts to bacterial products in the manner carried out by Thal and Brackney experimentally. Although several investigators have obtained sterile cultures from the pancreas in as many as 50 per cent of their cases and the gallbladder has been found to be normal in 30 of 125 cases of acute pancreatitis,[20] the bacteriologic aspects of this disease deserve to be carefully reinvestigated.

Vascular Factor.—In studies of pancreatitis a vascular factor also is frequently mentioned. Experimentally, arterial occlusion alone produces only focal lesions and not diffuse spreading pancreatitis.[30] The vascular factor does appear to be important, however, in the transition of edematous pancreatitis into pancreatic[15,31] necrosis and in the production of pancreatitis by the Shwartzman phenomenon as employed by Thal and Brackney.[14] The effect of vascular changes has been studied[32] in one hundred cases of malignant hypertension and although infarcts were found in seven cases and focal parenchymal necrosis in twenty-one cases, diffuse hemorrhagic pancreatitis or diffuse pancreatic necrosis was not observed in a single instance.

If arterial occlusion by itself were an important factor in the pathogenesis of this disease, it would be encountered frequently in cases of periarteritis nodosa and subacute bacterial endocarditis, but it is not.[33] Although infarcts are commonly found in cases of periarteritis nodosa or subacute bacterial endocarditis, I cannot recall a single case of this type in which the disease terminated with diffuse pancreatic necrosis.

Although arterial occlusion or vascular erosion may not be important in the initiation of the disease, it may be very important in the progression of the lesion. This was well illustrated in a case of acute pancreatitis reported by Gambill and co-workers,[34] in which erosion and thrombosis of a branch of the pancreatico-duodenal artery caused infarction of the body and tail of the pancreas. Observations like these have led me to the opinion that in most cases pancreatitis begins as acute pancreatic necrosis. Whether it becomes hemorrhagic or not then depends on vascular complications such as erosion or occlusion.

Alcoholism.—Another condition that is commonly emphasized as being of pathogenetic significance in most large series of clinical cases of acute pancreatitis is alcoholism.[3,34-38] Necropsy in cases of acute[36,39,40] and chronic alcoholism also has revealed a high percentage of pancreatic lesions including acute hemorrhagic pancreatitis. Clark[40] was impressed by the absence of disease

of the biliary tract in most cases. Carter[41] and Domzalski and Wedge[42] found that a high percentage of alcoholic patients had increased values for serum amylase, and they felt that alcoholics suffer from repeated mild or subclinical attacks of acute pancreatitis. Albrink and Klatskin[43] have reported the occurrence of marked but transient lactescence of serum in patients with abdominal pain after bouts of acute alcoholism. The evidence presented suggested that the hyperlipemia and abdominal pain were due to acute pancreatitis.

How does alcohol play a role in the development of pancreatitis? Pancreatitis has not been produced experimentally with alcohol in animals, but Egdahl[44] suggested that in human beings gastroenteritis produced by alcohol might be responsible for pancreatitis. Myers and Keefer[36] suggested three possibilities: (1) that alcohol in the blood might damage the pancreas directly, (2) that duodenal congestion or inflammation might obstruct the ducts, and (3) that persistent vomiting might cause regurgitation of the duodenal contents into the pancreatic ducts.

Rich and Duff[3] suggested that alcohol could produce pancreatitis by obstruction due to duodenitis and inflammation of the papilla associated with pancreatic hypersecretion. McGowan, Butsch and Walters[23] have shown that after the oral ingestion of alcohol, hydrochloric acid and alcohol cause spasm of the sphincter of Oddi. After large quantities of alcohol have been taken orally, edema of the duodenal mucosa and papilla of Vater also may occur. Dreiling, Richman and Fradkin[45] have suggested that the oral intake of alcohol causes the pancreas (via the secretin mechanism) to secrete a large volume of juice against an obstruction produced by spasm and edema of the papilla.

Malnutrition.—Recent reports offer still another possible role for alcohol in the etiology of pancreatitis,[46,47] namely, the protein and vitamin deficiencies that occur in chronic alcoholic patients. It has been suggested that the chronic undernutrition of alcoholic patients produces a situation analogous to that of ethionine pancreatitis. We have studied pancreatic lesions in a wide variety of conditions in which malnutrition is a feature including uremia,[48] obstruction of the small intestine[49] and carcinoma of the stomach, but in none of them has acute pancreatic necrosis or acute hemorrhagic pancreatitis been a feature. In these cases dilatation of acini, inspissation of secretion and atrophy were the prominent features, and vomiting and dehydration as well as malnutrition were considered to be contributing factors in producing the lesions.

In studies of fatal cases of chronic ulcerative colitis[50] and cirrhosis of the liver,[51] conditions also associated with malnutrition, these and other lesions, especially chronic interstitial pancreatitis, were commonly found in the pancreas, but it is not possible, in the light of present knowledge, to relate these changes to diffuse pancreatic necrosis. It is interesting that in a study of pancreatic lesions associated with cirrhosis of the liver[51] the incidence of these lesions was found to be higher in twenty-nine patients with histories of alcoholism than in others, but the number of patients studied was too small to be of statistical significance.

Postoperative Pancreatitis.—In most cases of postoperative pancreatitis the disease occurs after operations on the stomach and biliary tract.[52-56] Surgical manipulation and trauma to the pancreas occur most commonly in operations in this region. Not infrequently the duct of Santorini may be ligated, severed or injured, and the circulation to the pancreas may be impaired when the duodenum is mobilized during gastrectomy.[52] Sludging of pancreatic secretions incidental to medication, dehydration and vomiting may be a contributing factor that merits further investigation.[53] Reports from the literature suggest that operative investigation[54-56] of the common bile duct and cholangiography and use of the long-arm T tube[54] as well as sphincterotomy[57] are important factors in precipitating acute pancreatic necrosis. According to those who have studied serial determinations of serum amylase in patients after operation, the incidence of pancreatic disease as interpreted by this test is very high.[58] Perryman and Hoerr[59] indicated that a third of the patients had abnormal elevations of serum amylase. Most increases occurred after operations on the stomach and biliary tract.

Of particular interest are the cases in which pancreatitis occurred after operations far removed from the pancreas, such as, transurethral prostatic resection. In these cases, it has been postulated, that sludging of pancreatic secretions and release of proteolytic enzymes from resected prostatic

tissue play a role in imitating pancreatic necrosis.[60,61]

Pancreatitis that occurs during and shortly after pregnancy also is poorly understood and warrants further investigation.[17,62-64] In our own cases, and those reported in the literature, a high incidence of gallstones has been noted.

Summary and Conclusions

This review by no means exhausts the clinical and surgical conditions associated with acute pancreatitis and pancreatic necrosis, but perhaps enough has been said to emphasize the complexity of the pathogenesis of this disease of the pancreas. Although the experimental methods used to produce pancreatitis have done much to elucidate the pathogenetic mechanisms involved, it seems clear to me that most clinical, surgical and pathologic observations support the view that this disease is not the result of any one factor nor any one combination of factors, but that there are a great many factors and that they are often present in different combinations. In other words, the tissues and secretions of this organ respond in a similar fashion to a wide variety of injuries.

Every single case should be studied carefully from clinical, chemical, surgical and pathologic aspects, in order to learn more about the pathogenesis of this disease. Each case presents its own problems, and factors that may be of pathogenetic significance in one instance may not hold at all for the next one. For this reason the practicing physician and surgeon, by careful observation, can contribute greatly to our knowledge of this condition and can often indicate new methods for the experimentalist to use in approaching the problem.

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Modern Therapy in Diabetes Mellitus, Insulin, and the Oral Hypoglycemic Agents

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MODERN trends in drug therapy and clinical investigation have as a goal the delineation of specific drug action in contrast to the earlier forms of empirical therapy, which for the most part were symptomatic. This tendency is desirable if it results in the reversal or amelioration of the basic cause of a disease, but it may, on the other hand, be futile and misleading if specific symptoms are interpreted as wholly representative of the disease process. In this latter circumstance, an alteration of a symptom might be construed as a correction of the underlying pathologic process. A hypothetical example of the fallacy of such reasoning is use of a fever-reducing drug such as aspirin as the treatment for typhoid fever. It is more difficult to give examples when the underlying pathologic lesion or its etiology is less clearly defined. Does a drug which acts solely to lower blood pressure control the disease state called hypertension? And does a hypoglycemic drug ameliorate diabetes mellitus?

There has recently been greatly renewed interest in oral therapy of diabetes, which has been further stimulated by the availability of effective oral hypoglycemic agents. Opinions vary widely concerning the real value of this mode of therapy. Some authorities assume that diabetes is indeed improved, while others are equally emphatic that the underlying metabolic defect is not being repaired and that consequently, such treatment merely influences one laboratory manifestation, just as hyperglycemia can be reduced by artificially lowering the renal threshold by means of phlorhizin. Since evidence is not yet available to settle this controversy, it is hoped that this consideration of the problem may be helpful in both orientation and in the assignment of various therapeutic measures to their proper position in the management of this disease.

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Physiological Aspects of Diabetes

Diabetes mellitus is a hereditary disease characterized by permanent hyperglycemia and glycosuria and impairment of the body's normal ability to utilize food. The clearly defined metabolic defect is most strikingly illustrated by failure of peripheral utilization of glucose by skeletal muscle. That the immediate cause of diabetes is an actual or relative deficiency of endogenous insulin is established beyond question. Physiologic treatment consists essentially in compensating for this deficiency so that the diabetic taking an adequate diet can maintain his normal nutritional state and repair his tissues along normal metabolic pathways. In consequence, the blood-sugar level falls. In the untreated diabetic, however, hyperglycemia *per se* may, as some contend, actually reflect a compensatory mechanism essential to his survival and may even facilitate the utilization of glucose by the muscle cells.

The principles of treatment of diabetes have been established on the basis of the pathogenesis of the disease. Actual insulin deficiency can be produced by any mechanism which will deprive the body of its insulin-producing cells or inhibit their function. Surgical removal, or destruction of the islets by neoplastic infiltration, are relatively uncommon. Traumatic injuries to the pancreas are infrequent although damage by disease is known to occur. Experimentally, diabetes can be produced by the administration of cytotoxic chemicals such as alloxan,[1] which has a specificity for the beta cells of the pancreas, or by agents that overstimulate or sufficiently increase demands on these cells and ultimately exhaust them, such as, anterior pituitary extracts[2] (growth hormone), and a long continued plethora of glucose.[3] Similarly, substances capable of increasing the rate of insulin destruction (insulinase),[4] or those having a "block-

ing effect" (antibodies)[5] would be capable of causing diabetes.

Most cases of clinical diabetes fall into a different category and probably do not represent total insulin deficiency. Usually, it is more realistic to attribute the symptoms to diminished insulin production or interference with the rate of release of insulin by the beta cells, as proposed by Wrenshall, et al,[6] of Toronto. It was observed that in certain instances of diabetes the amount of insulin which could be extracted from the pancreas following its removal after death was not less than normal. Furthermore, in certain of these glands, the beta cell granules, which are assumed to be the precursor of insulin, appear to be larger than normal.[7] Wrenshall suggested that perhaps some release mechanism is at fault, which prevents the mobilization of the insulin.

Obesity, hyperthyroidism, hyperpituitarism, and overactivity of the adrenal cortex, are clinical factors which may overwork and ultimately damage the islet mechanism, resulting in an inadequate supply of insulin. These effects may be partially or wholly reversible and correction of the abnormality, be it a weight reduction or removal of a pheochromocytoma, not uncommonly serves to restore the deficiency, thereby permitting the metabolism of carbohydrate, protein, and fat to return toward normal.

There is considerable experimental evidence to support the theory that some types of diabetes may result from an increased destruction of insulin formed by the pancreas.[8] Insulinase, an enzyme which occurs naturally in the liver, has been found to be quantitatively increased in some diabetics. Such a patient might produce entirely normal, or even greater than normal, amounts of insulin, yet because of more rapid or more extensive destruction of the hormone a relative deficiency would develop.

Also, there may be other inhibitors of insulin as yet unidentified which could account for the apparent existence of a tissue barrier which is observed in certain cases of severe insulin resistance.

Action of Insulin

In the presence of insulin, certain physiological effects are measurable and can be shown to be specifically related to the action of the hormone itself. A catalytic action occurs in the Krebs cycle, which is the final common pathway for the oxidation of all foodstuffs to carbon dioxide and water.[9] Insulin is involved in the reversible reaction of glucose with adenosine triphosphate to form glucose-6-phosphate.

A second, and equally-important, function of insulin is its enhancement of the transfer of glucose across the cell membrane.[10] This action may be non-specific for glucose since it has been demonstrated with other sugars bearing a close structural relationship to glucose. Nevertheless, since glucose is the only sugar normally found circulating in the body fluids, the action appears to be specific *in vivo*. Other actions of insulin have been demonstrated; and, without dwelling on them extensively, it should be mentioned that insulin also accelerates the conversion of glucose to glycogen in muscle and liver, it accelerates the conversion of glucose to fatty acids in the liver and adipose tissue, and it is necessary for the oxidation of pyruvic acid to carbon dioxide and water. Finally, it is important in protecting the body against nitrogen wastage, insuring normal repair and growth.

As pointed out earlier, all these effects on assimilation and utilization of essential energy producing foodstuffs, glucose, protein, and fat, reduce the concentration of glucose in the blood and prevent glycosuria. Insulin permissively re-establishes normal metabolic pathways of utilization, and the effects are quantitatively measurable.

The clinical effects of absolute insulin deficiency are well known and clearly defined. In such deficiency, hyperglycemia and glycosuria actually represent only the first step in the failure in metabolism. Associated with such deficient utilization in the severe diabetic, there soon follows a reduction of glycogen stores in the liver, the muscle and the skin, other serious consequences of nitrogen imbalance, and finally, ketosis.

Since preservation of life is the first law of biology, the organism must call into play other abnormal or emergency mechanisms in its attempts to sustain a supply of energy to the cells. This alternate mechanism is based upon the utilization of fat and proteins and results in the production of ketones in the liver. Ketone bodies can be utilized as a source of energy by the cells in the absence of insulin,[11] a measure which is called upon in the first stages of starvation. Obviously it must be a temporary alternative, and, furthermore, since the production of ketones is not regu-

lated quantitatively, overproduction occurs far beyond the power of the cells to utilize it for energy. Acetonuria is a protective mechanism to excrete the excess ketone bodies.

As a result of protein breakdown, there is in addition a great increase in nitrogen excretion in the urine and the rapid establishment of a negative nitrogen balance. Acidosis and dehydration are soon established and since the ketone bodies combine with fixed base, there is also a fall in the carbon dioxide combining power and a shift of pH of the blood toward the acid side.

The toxic effects of the ketone bodies on the central nervous system include stimulation of the respiratory center, causing hyperpnea, or Kussmaul respiration, followed by coma, circulatory collapse, and ultimately, death. All of these effects can be reversed, short of death itself, by the judicious and vigorous administration of insulin.

Insulin Therapy

The efficiency of replacement of the actual or relative insulin deficiency in diabetes depends upon a smooth release of insulin having its availability proportional to physiologic demand. Soluble, quick-acting insulin is not the most efficient since its time-action is too abrupt and not sustained over a long enough period. Attempts to meet this need culminated in 1935-1936 with Hagedorn's[12] discovery of protamine insulin, which was further modified by the addition of zinc[13] in order to prolong the action over the period of nocturnal fasting. Later studies have provided modifications having peaks of release at the time of greatest need, namely, during the periods of heaviest metabolic load occasioned by food intake.

These developments in insulin modification have provided preparations of different time action. Protamine Zinc Insulin, Globin Insulin, NPH Insulin and, finally, Lente Insulin. Short of modifying insulin in such a way that its release from a subcutaneous depot would be regulated by the blood-sugar level (that is, so that hyperglycemia would effect its release while normo- or hypoglycemia would not), the modification of the time-action of insulin has advanced about as far as possible.

The next most obvious challenge lies in the development of an orally active substance which will effectively repair the underlying defect in diabetes. It is this problem that has proven to be a most difficult one.

Glycosuria and hyperglycemia are the most easily observed symptoms of diabetes, and, in addition, are objective in that they can be conveniently measured. They are regarded by both the doctor and the patient as criteria of control or lack of control of diabetes. Consequently, measures to combat excessive blood sugar have been classified as antidiabetic, and drugs that lower the blood-sugar level are called antidiabetic drugs. This term is fallacious, as pointed out by the Informational Committee on Oral Hypoglycemic Drugs of the American Diabetes Association.[14] Such drugs should only be classified as hypoglycemic compounds until it is shown that their effects on basic physiologic processes parallel those of insulin itself, and that they establish a fall in blood sugar as a result of these actions and not merely an unrelated or even toxic incidental effect. It is obvious from the voluminous investigative effort already expended in research on the mode of action of the oral hypoglycemic agents that the problem is not to be easily solved.

Oral Hypoglycemic Agents

Over the years a great number of orally-administered compounds have been tested for their effects on the blood sugar. Some, like myrtillin, apparently had no actual measurable effects under control conditions, and others, like synthelin, were soon found to be too toxic for continued clinical use. A third type of drug, such as phlorhizin, simply lowered the renal threshold to glucose, thus permitting a massive excretion of glucose, reducing glycemia in a manner analagous to lowering blood pressure by continuous bleedings. Blood sugar may indeed be lowered by several means which obviously could not be interpreted as favorable to the longevity of the diabetic himself, for example, hepatectomy as cited by Stetten.[15]

Other and new approaches have recently led to the development of another class of drugs having blood-sugar lowering properties. In 1942, Janbon[16] published the first report of induced hypoglycemia in man following the oral administration of a sulfonamide derivative. This was followed by work of other investigators, including Bovet and Dubost,[17] in 1944, Loubatieres,[18] in 1944, and Chen,[19] in 1946, who studied similar compounds. Unfortunately, all of these compounds were found to

TABLE I. REACTION INCIDENCE

Forms Returned	1319
Cases Reported	7193
Side Reactions	389
Reactions Per Cent	5.36

TABLE III. UNEXPLAINED FATALITIES

Sudden Myocardial Failure	1
Sulfonamide Sensitivity	2
Bone Marrow Depression	1
Dermatitis Exfoliative	1
Acute Pulmonary Edema	1
Liver Involvement	2

TABLE II. REACTION CLASSIFICATION
(NUMBER OF CASES)

Rash	109	Thrombocytopenia	2
Anorexia, Nausea, Vomiting	81	Purpura	2
Malaise, Lethargy, Fever	79	Eosinophilia	2
Agranulocytosis, Leukopenia	58	"Headache"	2
General Allergy	25	Psychosis	1
Cardiovascular, Renal	16	Hypothyroidism	1
Exfoliative Dermatitis	6	Methemoglobinemia	1
Acute Anemia	6	Tachycardia	1
Jaundice, Liver Function	6	Sudden Myocardial Failure	1
Acute Edema	4	Unclassified	10
Crystalluria	3		

cause liver and kidney damage which precluded their use in the treatment of diabetes.

Early in 1954, two German investigators, Franke and Fuchs,[20] reported that a new soluble sulfonamide derivative, designated BZ-55, exerted a hypoglycemic effect in normal and certain diabetic patients, without evidence of acute toxicity. Their work was extended to include a series of diabetic patients,[21] and in 1955 investigative programs were established in the United States[22] which included not only this compound, termed carbutamide in the United States, but also a second German compound designated tolbutamide.

Chemically, these compounds are classified as sulfonamide derivatives, and since they were representatives of a family of drugs which had been used extensively in medicine, it seemed that they held promise as possible effective agents in diabetes.

The clinical trial investigation of BZ-55, or carbutamide, as it had been designated, was one of the largest ever attempted by a pharmaceutical manufacturer. During the period from July, 1955, to October, 1956, the drug was made available to more than 2,900 investigators for evaluation in approximately 10,000 diabetic patients. Such a broad-scale trial was deemed necessary for two basic reasons. Although toxicity had been reported to be quite small, nevertheless, the compound did bear a relationship to other sulfonamide derivatives which have been known to cause toxic side reactions. Furthermore, since the administration of the drug would be continuous over a period of years, there was no satisfactory way of determining the possible harmful effects from chronic administration. Therefore, a broad trial seemed to be the only practical method of assessing the incidence of acute and chronic toxicity and evaluating the real usefulness of the compound.

Within a short time a number of facts became known. First of all, carbutamide had limited application and was effective in only certain types of diabetes, while it did not protect at all against serious manifestations, as ketosis, relapse in infections, and prevention of nitrogen wastage. Secondly, and more important, evidences of toxicity became apparent.

In July, 1956, information was received about three unexplained deaths in patients taking carbutamide. In each instance the possibility that the administration of carbutamide may have contributed to the findings demonstrated at autopsy could not positively be excluded. Analysis of the clinical trial reports in September revealed a total of eight of these unexplained fatalities and an over-all reaction rate of 5.36 per cent[23] (Tables I, II, III). While it was true that the vast majority of side reactions were relatively minor and usually reversible as soon as therapy was stopped, on the other hand, the deaths could not be disregarded. At this time evidence was also received from the Toronto laboratories of Dr. Charles Best[24] which indicated that liver damage had been demonstrated in depancreatized animals maintained on both carbutamide and insulin. Similar findings were reported from Denmark.[25]

In view of the serious side-effects, and the fact that in most patients oral treatment is merely an optional alternative form of therapy of convenience rather than necessity, the broad clinical trial of this drug was suspended on October 26, 1956.

From the standpoint of toxicity, the experience reported with tolbutamide has been much more favorable.[26] So far, no deaths have been reported and, apparently, the incidence of side reactions is considerably less. Nevertheless, there is general agreement that the mode of action of both compounds is the same, although there is some evidence that the drug is less effective. This raises another important question—is effectiveness interrelated with toxicity?

The advantages of oral therapy are quite apparent. First, the patient taking the drug can forego

the daily injection of insulin. If not previously taking insulin, hyperglycemia and glycosuria may be reduced in patients who could not previously be successfully managed by dietary restriction alone. The factor of convenience, while it must not be disparaged, especially from the patient's standpoint, must be examined critically before it can be accepted. A review of the present knowledge about mode of action of these drugs may be helpful.

Action of Sulfonylureas

To be a true substitute for insulin, a proposed agent should be able to correct the fundamental defects in metabolism which are associated with the clinical syndrome called diabetes mellitus. Unquestionably, the sulfonylureas do not meet these criteria. Clinical and experimental evidence indicates decisively that in the total diabetic, either in animals or in humans, no adequate lowering of blood sugar can be obtained. It is absolutely necessary that some pancreatic function be present before a measurable lowering of the blood sugar can be produced by these compounds. Several theories of action can be advanced.

As a first consideration, the effectiveness of available insulin could be increased through any one of several mechanisms—by increasing the peripheral utilization of glucose by some mechanism independent of insulin itself, by influencing liver glycogen levels, by inhibiting insulinase, or by stimulating the output of insulin from the beta cells.

It would seem logical that if these drugs increased the effectiveness of the available insulin, that this insulin effect would be measurable in the peripheral tissues.

The experimental evidence available up to the present time is contrary to this concept. The following summary is from the report of a committee who reviewed the present knowledge of the effects of the sulfonylurea compounds.[27] There is no evidence of blood-sugar lowering in eviscerated dogs (Levine), rabbits (Wick), or rats (Ingle), either in the absence of or with supplemental insulin present. Furthermore, there is no change in glucose uptake by the isolated rat diaphragm or in rat adipose tissue where insulin has a marked effect (Krahl, Cahill, Clarke, Field). Finally, in this regard, there is no increase in arteriovenous difference after glucose loading (Goldner).

Data presented to show an effect on liver glycogen is somewhat confusing. In part this may be attributed to variations in experimental design. Evidence has indicated that the sulfonylurea compounds inhibit the output of glucose from the intact liver and, specifically, of that derived from fructose and galactose (Renold, Craig). On the other hand, liver slice studies indicate that the addition of these compounds to the medium does not inhibit glycogenolysis or glucose output (Cahill, Sutherland).

While the glycogenolytic effect of glucagon and epinephrine in liver slices may be inhibited by the drugs (Vaughn) and in the intact animal glucose release by these agents may also be inhibited (Izzo), this latter finding could not be confirmed by others (Fajans, Anderson, Goldner).

In vitro inhibition of insulinase has been positively demonstrated (Mirsky) but *in vivo* experiments indicate that blood levels of the compounds do not reach a level sufficiently high to confirm these findings. Furthermore, when similar concentrations are used in isolated liver preparations, there was no significant reduction of insulinase activity (Vaughn, Williams).

Early in the experience with these compounds it was proposed than an inhibition of the alpha cells of the pancreas with a diminution of glucagon output could account for the blood-sugar lowering effects. The bulk of the present evidence fails to support this theory.[28]

Finally, the stimulation of the release of insulin from the pancreas could also increase blood-sugar lowering and it has been demonstrated that amounts of carbutamide infused into the arterial supply of the pancreas resulted in a fall in the peripheral blood-sugar level in amounts approximating 20 per cent (Colwell).

Cross circulation experiments indicate that blood from the pancreaticoduodenal vein but not the mesenteric vein of the dog treated with carbutamide resulted in a fall in the blood sugar in the recipient (Foa).

Although these latter findings seem to indicate that there must be some stimulation of insulin release, the failure of the drugs to alter blood glucose in a manner known to be associated with insulin injection is inconsistent with this hypothesis. V. Holt's later observations[29] indicating a stimulating effect of carbutamide on insulin activity, followed by a relative insufficiency and

TABLE IV. COMPARISON OF INSULIN AND ORAL SULFONYLUREAS

	Insulin	*Sulfonylureas*
I. *Indications*		
(a) All diabetic children	Yes	No
(b) Severe cases of diabetes	Yes	No
(c) Complications of diabetes	Yes	No
Acidosis	Yes	No
Surgery	Yes	No
Emergencies	Yes	No
(d) Diabetes in pregnancy	Yes	No
(e) Mild diabetes in elderly obese patient not controlled by diet	Yes	Yes
II. *Effects*		
(a) Antidiabetic	Yes	No
(b) Hypoglycemic	Yes	Yes
(c) Promotes utilization of carbohydrate and fat in a normal manner	Yes	Evidence Controversial
(d) Maintains normal nitrogen balance	Yes	Unknown
(e) Quantitative dose-response	Yes	No
(f) Physiological lowering of blood sugar	Yes	Unknown
(g) Eliminates ketosis	Yes	No
III. *Actions*		
(a) Physiological replacement	Yes	No
(b) Deficient islet cells stimulated There is some concern as to whether or not stimulation of deficient islet cells may eventually result in exhaustion of the already deficient insulin production.	No	Probably yes
(c) Liver cells protected	Yes	Unknown
(d) Liver metabolism interrupted	No	Possibly
(e) Restores peripheral utilization of glucose	Yes	Controversial
(f) Insulin secretion stimulated	No	Possibly
IV. *Toxicity*		
(a) Hypoglycemia	Yes	Yes
(b) Drug allergies	——	Yes*

*Drug allergies—reported effects on skin, bone marrow, liver. Long-term effects still in question.

decrease in sugar tolerance, and increase in liver glycogen of fasting animals along with other inconsistencies, seem to point to a different mode of action.

From the foregoing necessarily brief review of the physiologic effects of the oral sulfonylureas, it can be seen that in many crucial aspects, the action of these drugs can not be compared favorably with insulin. The only clearly positive fact presently available is that the blood sugar can be lowered, but this effect is a result of actions as yet not clearly defined. The following table (Fig. 4) of comparison may help to clarify the differences.

Critical Appraisal

Editorial comment relative to the clinical use of these compounds has been unanimously conservative. The American Diabetes Association presented a number of questions pointing out the shortcomings[30] and stated that "at the moment it seems as if they (the sulfonylurea drugs) are most effective where we do not need them, namely, in the adult who is overweight and mildly diabetic. The sick, acidotic diabetic patients still need Insulin," and further, "the education of the physician and the patient towards effective management of diabetes is the finest form of regulation that medicine has offered for any disease. It is not yet in the interest of good medicine and the well-being of diabetic patients to support the release for marketing of an 'insulin substitute' before adequate clinical testing and appraisal have been completed."

In the monograph appearing in the New and Nonofficial Drugs Section of the J.A.M.A. for July 20, 1957,[31] the secretary of the committee pointed out that the chief hazard will be the high incidence of ketosis during the transfer from insulin because certain patients are not suitable candidates for such conversion, and, furthermore, that "it should always be borne in mind that the only real advantage . . . over insulin is its effectiveness when given orally and that insulin remains the indispensable drug of necessity in all diabetic complications." Stetten commented[15] that since these drugs should be reserved for the treatment of those diabetic patients who fail to go into ketosis when insulin is withdrawn, such a statement is almost tantamount to saying that these drugs will control the symptoms of diabetes in the symptom-free diabetic patient, and until more is known about the mode of action, it will be difficult, in his opinion, to know with assurance whether or not we are doing the diabetic patient a favor when we lower his blood-glucose concentration by the administration of a drug of the sulfonylurea group.

Summary

Diabetes mellitus is a complex disease manifesting many alterations in metabolism which can be reproduced experimentally and measured. Insulin, the physiologic therapeutic agent, will reverse each of these abnormal processes regardless of the state of the severity of the diabetes. As a result of this reversal there is a disappearance of abnormal symptoms and also, a return towards normal levels of the blood sugar with the disappearance of glycosuria. So far the oral hypoglycemic agents presently undergoing study will measurably alter the blood-sugar level and the glycosuria in certain, but not nearly in all, selected diabetic patients. With these exceptions, they fail to meet in any way the criteria of an insulin substitute. So long as the compounds are used with full understandings of their limitations it can be presumed that they are useful measures

in a limited group of diabetics, but whether this usefulness will prove to be a two-edged sword remains to be seen.

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JOINT ASSA-AHA SESSIONS

A program which includes a symposium on "Genetic Factors in Cardiovascular Disease" and panels on the subject of arteriosclerosis will be presented jointly by the American Society for the Study of Arteriosclerosis and the American Heart Association at the AHA Scientific Sessions in San Francisco, October 24-26. This year, for the first time, the American Society for the Study of Arteriosclerosis is holding its annual meeting to coincide with the American Heart Association's scientific sessions.

The joint ASSA-AHA program opens Friday morning, October 24, with a symposium, "Genetic Factors in Cardiovascular Disease," Dr. Victor A. McKusick, Baltimore, and Dr. David Adlersberg, New York, Chairmen. Sessions on the following subjects will be included: "Hypertension," with Sir George Pickering, Oxford, England, Dr. Caroline B. Thomas, Baltimore, and Dr. Douglas R. Drury, Los Angeles, participating; "Atherosclerosis," with Dr. Arthur G. Steinberg, Cleveland, Dr. Frederick H. Epstein, Ann Arbor, Michigan, and Dr. Richard H. Osborne, New York; "Rheumatic Fever," with Dr. May G. Wilson, New York and Dr. Paul A. Lembcke, Los Angeles; and "Congenital Malformations," with Dr. Catherine A. Neill, Baltimore, and Dr. McKusick. Discussion will be opened by Dr. Antonio Ciocco, Pittsburgh.

Panels will be held on Saturday afternoon, October 25, on "Emotional Factors in Atherosclerosis," with Dr. Louis N. Katz, Chicago, Moderator; and "Hypertension and Atherosclerosis," Dr. A. C. Corcoran, Cleveland, Moderator.

Cysts of the Spleen

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CYSTS of the spleen are rare, representing the least frequently encountered cystic disease involving abdominal viscera. The first reported case of a splenic cyst was a dermoid reported by Andral,[1] in 1829. The first splenectomy because of cyst was performed by a French surgeon, Péan,[2] in 1867. Surgical interest in splenic cysts was aroused in this country by Fowler,[3] whose first article on the subject appeared in 1910. He maintained an active interest in this problem until his death, and his scholarly articles[4-7] did much to clarify the nature of the condition.

Present Study

The work of Fowler and others stimulated us to review the experience with splenic cysts at the Mayo Clinic. We first took a sampling from the records in our files to determine the incidence of splenic cysts and then restricted our study to those cases in which the spleen was surgically removed because of cystic disease and in which the clinical records, as well as gross and microscopic sections, were available for investigation. These cases were subjected to a detailed clinical and pathologic study.

Results

During the years 1935 through 1952, a total of 1,283 splenectomies were performed at the clinic. One or more cysts were present in fourteen of these spleens, an incidence of 1.09 per cent.

The first splenectomy done at the clinic because of a cyst was performed by Dr. W. J. Mayo, in 1911; only eighteen additional cases were encountered in the subsequent years through 1956. This total of nineteen cases comprises the basis of our study. These cases were divided into two groups. The first group consisted of the five cases in which the cysts were small (5 cm. or less in diameter); the second group consisted of the remaining fourteen cases in which the cysts were larger than 5 cm. The largest cyst measured 30 cm. in diameter.

The ages of these nineteen patients ranged from eleven to sixty years, with an average of thirty-two. The sex distribution in this series was eleven females and eight males, which confirmed the findings of other observers that cysts of the spleen occur more frequently in the female. However, the suggestion that formation of splenic cysts may be related to pregnancy and abnormal menstruation was not borne out.

Trauma has been mentioned as a cause of cyst formation in the belief that these lesions are often simply encysted hematomas. Histories of trauma were obtained in four of these cases, but it appeared extremely questionable that this factor was the primary cause of the cysts. The mass had existed for two years in one case, but just prior to operation it had enlarged rapidly after trauma. The findings in this instance substantiated the occurrence of recent hemorrhage into an already existing cyst; it appears likely that this is often the case.

Malaria and syphilis as causes of splenomegaly, together with the supposition that such enlarged spleens are more vulnerable to trauma and subsequent formation of cysts, were not established in this study.

We could find no sign or symptom attributable to the small cysts. However, in the group of large cysts, two clinical features were present in all but two cases. They were a palpable mass in the left upper quadrant of the abdomen and pain in that same region. These two features occurred separately or in combination; however, more frequently than not they occurred together.

One of the questions we wished to answer was whether splenic cysts were ever the cause of hematologic disorders. The group of five cases in which small cysts were present included two

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cases of hypersplenism, a case of congenital hemolytic anemia and one of essential thrombocytopenic purpura. However, we could not incriminate the cysts as being the cause. Evidence of hematologic disease was absent in the group of large cysts.

the relationship of the cysts to the splenic capsule.

Capsular Cysts.—Five of the nineteen surgical specimens exhibited small, thin-walled cysts that

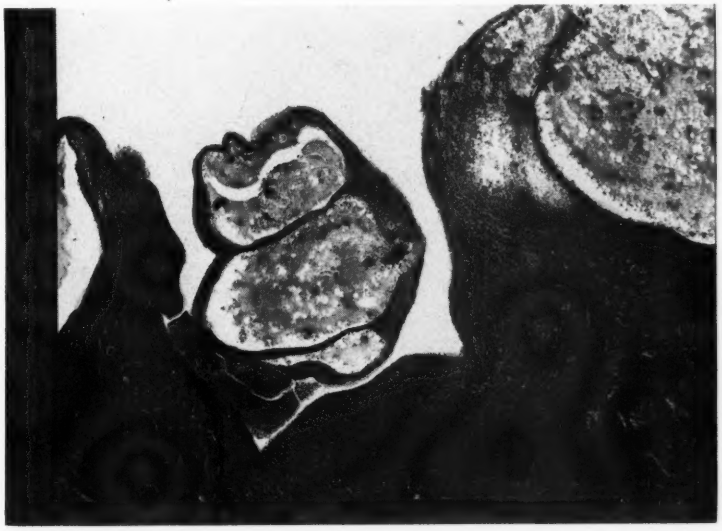

Fig. 1. Typical example of capsular or subcapsular splenic cysts. These cavities, usually multilocular, as in this instance, are filled with a coagulum and lined by a single layer of endothelial or mesothelial cells (hematoxylin and eosin; x30).

The diagnosis was made preoperatively in only two cases. However, splenic cyst was considered in the differential diagnosis in three other cases. Roentgenologic examination offered the most help in preoperative diagnosis. A plain roentgenogram of the abdomen was obtained in ten cases and revealed a large, soft-tissue mass in every instance. Excretory urography was done in five cases and disclosed downward displacement of the left kidney in all five. Roentgenologic examination of the stomach after a swallow of barium was done in five cases, and displacement of the stomach to the right was evident in all. The information gained from these examinations should direct one to a diagnosis of splenomegaly, and a "cystic feel" on palpation might suggest that the splenomegaly was due to cystic disease.

The treatment in these cases was splenectomy, and this is probably the treatment of choice in all instances. There were no deaths in this series.

Pathologic Features

Pathologically, it appeared practical to subdivide the group into two categories, depending on

were multiple in four instances and that apparently arose from elements within or subjacent to the splenic capsule. None of these cysts had been palpable clinically, and, although splenectomy had been performed in two instances for hypersplenism (purpura and hemolytic icterus, respectively), it was not considered that the cysts themselves had contributed to the symptomatology in either instance.

All these capsular cysts appeared on the anterior margin or upper surface of the spleen. Their dimensions ranged from microscopic locules to fluid-filled spaces, the largest of which measured 2, 3, 4, 15 and 5 cm., respectively. The majority were thin-walled and filled with watery fluid, but several contained a dark, bloody, liquid material and exhibited thick walls. One such thick wall contained zones of calcification. Microscopically, the lining cells were plump, spindled and single-layered. This finding, along with a content of thin but sometimes coagulated, pink-staining fluid, suggested an origin from capsular lymphatic spaces or from sequestered clefts of peritoneal mesothelium (Fig. 1). Occasional erythrocytes

had found their way into these cysts, but none of the lesions was truly hemorrhagic.

Parenchymatous Cysts.—In the remaining fourteen cases, the cysts were parenchymatous with

Perisplenic adhesions were present in eight of the fourteen specimens in this category. They were so dense in three cases as to have posed major obstacles to splenectomy.

The cysts were solitary in twelve cases. In the

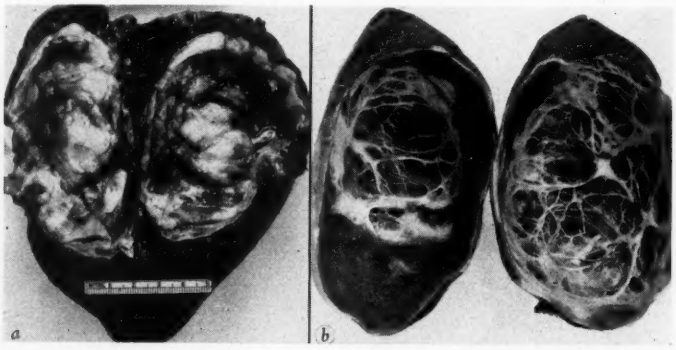

Fig. 2. *(a)* Splenic dermoid cyst, showing thick capsule and whitish lining of epidermis. *(b)* The fibrous, coarsely trabeculated walls of seven parenchymatous cysts appeared similar to this.

Fig. 3. Large parenchymatous cyst of spleen filled with old and recent blood clot.

respect to the site of origin. As already indicated, all these spleens had been large and symptomatic, being easily palpated in most instances. Weights of the intact specimens ranged from 100+ gm. to 4,235 gm., with the majority weighing in excess of 500 gm. Sizes ran from 8 by 7 by 7 cm. to masses exceeding 30 cm. in diameter.

remaining two cases, the entire spleen appeared to be involved in a diffuse process that had produced bosselations over the entire surface.

Contents of the cysts were "soupy" or "grumous" in the one example of a splenic epidermoid tumor (Fig. 2*a*). The two large spleens that were bosselated exhibited spongy and honeycombed surfaces that bled profusely. The gross appearance in these two spleens suggested cystic degeneration in basically solid tumors. The remaining eleven cysts, all unilocular, were filled with blood-stained or frankly bloody material in ten instances and with clear fluid in one.

After the contents of the cysts were washed out, the walls of the cavities were found to be coarsely trabeculated (Fig. 2*b*) in seven cases and smooth or uncorrugated in the remainder. In ten instances, a rind of tough fibrous tissue formed a wall or capsule for the cyst; in several cases, this otherwise white capsule disclosed dark zones resulting from ancient or recent hemorrhage (Fig. 3).

Microscopically, the diagnosis as to subtype was easy in the one epidermoid cyst (Fig. 4*a*). Likewise, the two bosselated tumors were typical examples of diffuse splenic hemangiomatosis with secondary cystification (Fig. 4*b*). Six of the remaining eleven parenchymatous cysts exhibited fairly uninterrupted linings with single or several layers of plump endothelial-like cells, which

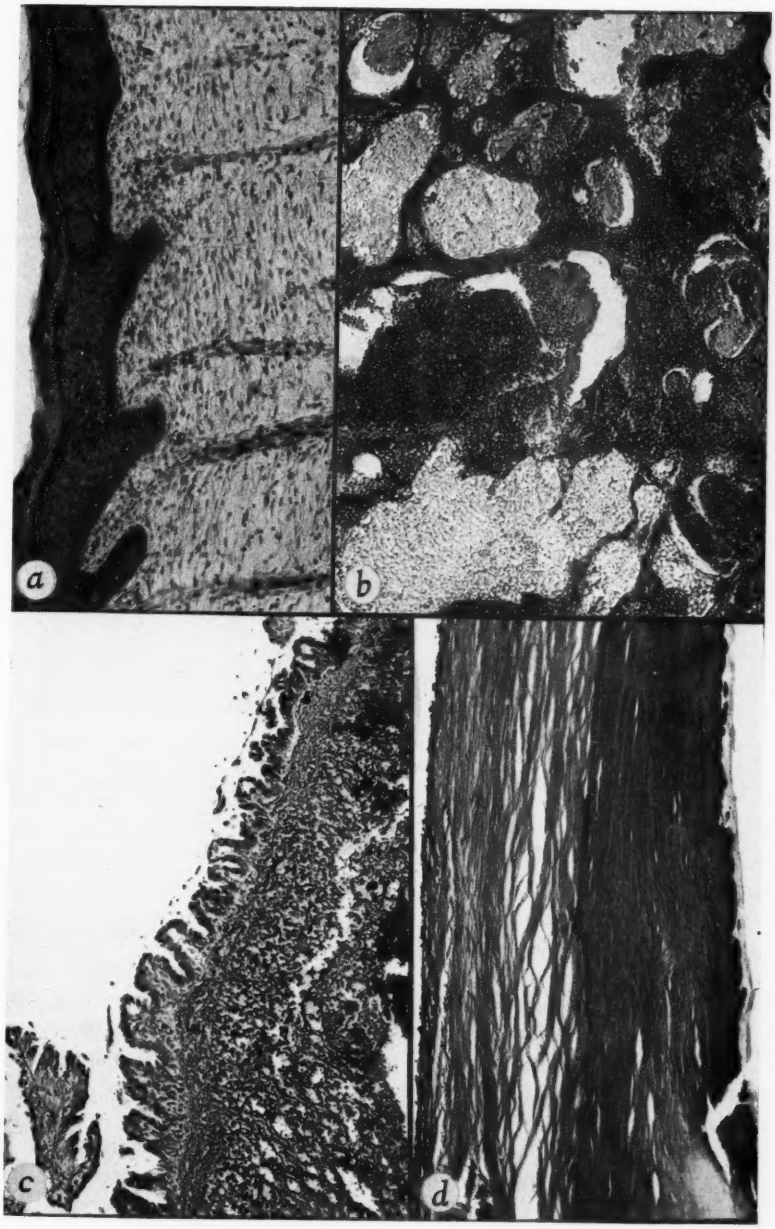

Fig. 4. Parenchymatous splenic cysts (hematoxylin and eosin). *(a)* Lining of cyst in Figure 2*a*, showing a thick layer of keratinizing epithelium with an underlying band of fibrous tissue (x100). *(b)* Splenic "hemangiomatosis." Cyst formation in the two cases displaying this feature was obviously degenerative in character (x50). *(c)* Papillary infoldings were a feature in one of six cysts whose linings appeared to be endothelial. This is the only instance in which the cells appeared to be proliferating (x100). *(d)* Thick fibrous linings, such as this, were features in five of the parenchymatous cysts (x100).

appeared to be proliferating in one case (Fig. 4*c*). In the remaining five cysts of this group, either a purely fibrous lining (Fig. 4*d*) existed or a fibrous lining was present that was interrupted here and there by zones wherein a few spindle cells were arranged in tandem to form a covering mantle.

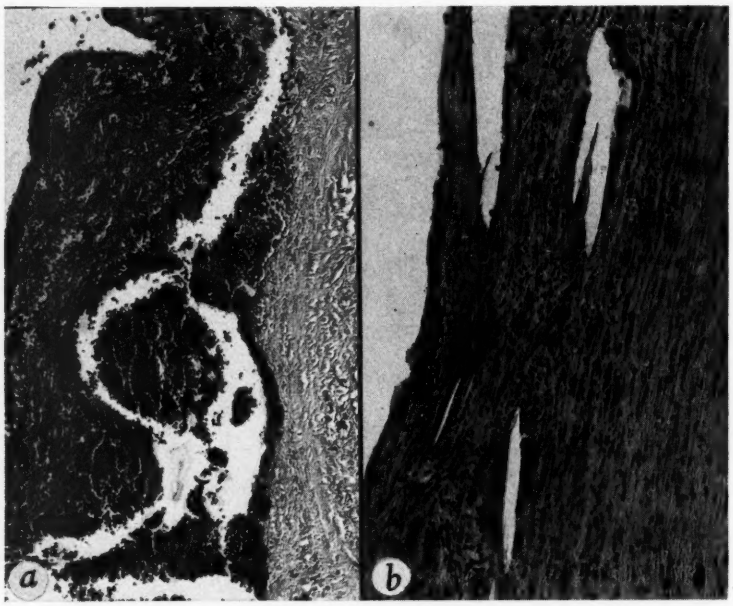

Fig. 5. Parenchymatous splenic cysts (both, hematoxylin and eosin; x100). *(a)* Dissecting through a fibrous investment are zones of old and recent hemorrhage. *(b)* Cholesterol-crystal clefts are hallmarks of recent hemorrhage.

Microscopically, the fibrous investment just described varied tremendously in thickness and in its complement of fibroblasts. In some cysts, it was thin, rather rich in young fibroblasts and almost lacking in collagen, whereas it was thick, acellular and almost completely hyalinized in others. Hemorrhage and impregnation with hemosiderin were evident in most lesions (Fig. 5*a*). Cholesterol-crystal clefts surrounded by foreign-body giant cells were noted in five cases (Fig. 5*b*).

The splenic parenchyma adjacent to the capsule of the cysts often appeared to be compressed. Farther away, the splenic sinusoids in a number of instances appeared to be so numerous and so dilated as to suggest the diagnosis of hemangioma, were it not for the finding of scattered malpighian corpuscles. These sinusoids frequently were lined by plump endothelial cells in a picture reminiscent of that seen in Banti's disease. An increased weight of true splenic tissue in these cases strongly suggested that the contained cyst had been exerting pressure on the splenic vein, with resulting splenomegaly.

Summary and Conclusions

A study has been made of nineteen cystic spleens surgically removed at the Mayo Clinic over a period of forty-six years. These nonparasitic cysts of the spleen were divided into capsular types (five cases) and parenchymatous types (fourteen cases). The former are multicentric, small and clinically unimportant. Pathologically, they appear to be derived from lymphatic spaces or peritoneal mesothelium. The parenchymatous category includes epidermoids, cystic hemangiomas and large unilocular cysts of uncertain origin. To label the latter "true" or "false," depending on the presence or absence of an "endothelial" lining, is impractical since many of the cysts would be labeled "true-false" by this criterion.

(Continued on Page 641)

Female Pseudohermaphroditism—The Adrenal Genital Syndrome

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FEMALE pseudohermaphroditism, a clinical entity, according to Young[1] was first described in 1865 by an Italian Crecchio who reported the case of a patient baptised as a girl but later thought to be a boy and reared as a boy. Twice this individual contracted gonorrhea. The physiognomy was that of a male. The breasts and nipples were small, the chest was hairy, the "penis" was six centimeters long and no testicles were palpable. The patient died at the age of forty-three years. Autopsy disclosed a uterus, tubes, and small ovaries. The adrenals were described as hypertrophied.

For many years accurate diagnosis of this condition was impossible and its clinical management had no foundation and was utterly confused. Now the confusion is resolved, accurate diagnosis is possible and clinical management is rationalized.

A pseudohermaphrodite is defined as a person in whom the gonads of only one sex are present but with abnormalities of the external genitalia which give doubt as to sex. In many of these persons secondary sex characteristics are the opposite of those in keeping with the gonads present and add to the uncertainty as to true sex.

The recent work of Wilkins and his co-workers[2] has done much to clarify this subject and make possible early accurate diagnosis and proper management.

The adrenal genital syndrome is a part of hyperadrenal cortisism. Manifestations of this may be divided into two main groups: (1) those with manifestations of the adrenal genital syndrome and (2) those presenting Cushing's Syndrome.

Children presenting the adrenal genital syndrome show excessive masculinization, accelerated epiphysial ossification, rapid but early terminated growth due to precocious muscular development and increase of the urinary 17 ketosteroids. In contrast, children of the Cushing's Syndrome have retarded growth, poor musculature, osteoporosis and obesity.

The adrenal genital syndrome may be due either to adrenal cortical neoplasm or to adrenal hyperfunction. The clinical manifestations of this syndrome vary with sex and the age the disorder begins. We are concerned here only with true sex females. The congenital form is due to fetal adrenal cortical hyperfunction. The postnatal form is due to either neoplasm or acquired adrenal cortical hyperfunction.

The work of Wilkins and his co-workers[3] in the administration of cortisone has proved of value not only in the treatment of hyperfunction but also as a diagnostic aid in differentiating adrenal hyperfunction from neoplasm. Wilkins has shown that the administration of cortisone causes a marked decrease in the output of urinary 17 ketosteroids in cases of hyperfunction but no decrease in the urinary 17 ketosteroids in those cases due to neoplasm. In addition to rapid growth, abnormal muscular development, and accelerated epiphysial ossification with increased urinary 17 ketosteroids these individuals are afflicted by a disturbance of electrolyte balance, with a tendency to a loss of sodium and elevation of serum potassium which may cause early death due to dehydration and circulatory collapse. Occasionally some of these individuals have hypertension without any abnormality of electrolytes. It is believed that enlargement of the adrenals when demonstrable is caused principally by hyperplasia of the reticular zone which is thought to be responsible for the secretion of androgen.

When female pseudohermaphroditism begins in embroyonic or fetal life, abnormalities of sex differentiation may be obvious at birth. There is hypertrophy of the phallus (clitoris) which resembles a penis with accompanying hypospadias. Often there is a persistent urogenital sinus which communicates ventrally with the urethra and dorsally with the vagina, uterus, and tubes. The appearance of the external genitalia varies consid-

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erably depending upon the degree of separation or fusion of the labial folds. The diagnosis of female pseudohermaphroditism due to congenital adrenal hyperfunction cannot be based on these findings alone because the same anatomic abnormalities may occur in individuals who have either testes, ovotestes, or ovaries.

TABLE I. DIFFERENTIAL DIAGNOSIS OF ADRENAL HYPERPLASIA AND TUMOR IN FEMALE PATIENTS

	Abnormality of Embryonic Sex Differentiation	Evidence of Excessive Androgen			
		Increased 17-KS	Excessive Growth and Osseous Development	Precocious Sexual Hair	Response of 17-KS to Cortisone
Congenital adrenal hyperplasia (female pseudohermaphroditism)	Hypertrophied clitoris Persistent urogenital sinus (usually)	+	+	+	+
Genetic intersexes with testes, ovotestes, or ovaries	Various abnormalities (including the above)	0	0	0	0
Postnatal Adrenal tumor	Normal at birth later virilization and hirsutism	+	+	+	0
Adrenal hyperplasia	Same	+	+	+	+
Constitutional hirsutism or "premature pubarche"	None	0 or + −	0	+ −	0

As shown in Table I (from Wilkins) congenital adrenal hyperplasia is accompanied by increased 17 ketosteroids and other evidence of excessive androgens while genetic intersex (true hermaphroditism) is not accompanied by increase of urinary 17 ketosteroids or other evidence of excessive androgen output.

Clinical Management

Proper management of female pseudohermaphroditism will be dictated by the age of the patient when the anomaly is clinically recognized. In this connection, in the cases of newborns *immediate* determination of the true sex is of paramount importance.

By endocrine therapy the true female may be put on the road to development of normal female secondary sex characteristics, the genital anomaly may be surgically corrected, and life in keeping with the true sex may be made possible.

If the adrenal genital syndrome is not arrested by endocrine therapy and the individual is allowed to develop male secondary sex characteristics, male conduct, identification as a male and male relationship to environment the process cannot be reversed. In this event, the true female must be allowed to follow the male life dictated by her endocrine anomaly with benefit of what help surgery can give: removal of uterus, tubes, ovaries, correction of hypospadias, implantation of plastic spheres in the labia (scrotum) and all else which may help the masquerade. Most important of all, when possible, she should be kept ignorant of the masquerade.

When this anomaly is suspected from appearance of the external genitalia of a newborn the true sex may be readily determined.

The work of Moore[4] on sex determination by skin biopsy and that of Greenblatt[5] by oral mucosal smears has made this early accurate diagnosis possible. No longer is exploratory laparotomy necessary.

From examination of skin biopsies from fifty females and fifty males of normal sexual development a difference in nuclear structures according to sex was demonstrated in cells of the malpigian layer of the epidermis. Nuclei of specimens from females contained a mass of sex chromatin which was seldom seen in the nuclei of specimens from males. The XX chromasomes of the female produce a chromatin mass sufficiently large to be identified while the XY chromosomes of the male fail to produce a chromatin mass of sufficient size to be distinguished from the general particulate chromatin.

This method of detecting the chromosomal sex of an individual was applied to two cases of hermaphroditism. One case proved to be a chromosomal female and the other a chromosomal male. Correctness of these histological diagnoses was verified by later developments and findings.

The same principles are used in determining

the genetic sex by histologic examination of scrapings of the oral buccal mucosa.

At present, examination of peripheral blood smears promises to be of value in determination of true sex.

Female pseudohermaphroditism in a high proportion of cases is the result of progressive androgenic overactivity of the adrenal gland during and after fetal life. This influence, in contrast with genetic, developmental or maternal influences in the case of other forms of pseudohermaphroditism, will continue to act after the period of fetal development. Progressive masculinization after birth can, therefore, be expected in these individuals. A female pseudohermaphrodite can be surgically and psychologically treated beginning in infancy with the result of fitting her to a female way of life, but she will have and will continue to have in some degree the secondary sex characteristics of a male: deep voice, masculine physique, beard, hairy body, and receding hair line of scalp. Because of these progressive changes which at present are irreversible by surgical or hormonal means she will be accepted neither as a male, nor a female.

Inevitable progression of masculinization disputes the thesis that all pseudohermaphrodites should be treated according to their gonadal sex.

At the age of approximately two or three years four criteria will allow determination of the degree to which masculinization has progressed.

They are (1) advance of bone age, (2) increased size of phallus (clitoris), (3) hirsutism and (4) elevation of 17-ketosteroid excretion.

Depending upon the degree of masculinization present, decision must be made as to the direction of clinical management—whether the child is to be a masculinized female or whether the child is to be a sterile male with ovaries. Even though it seems preferable to raise the child as a female, clitoridectomy should be deferred until puberty to be certain that the factors favoring ultimate feminization will still be present. Partial adrenalectomy and estrogen therapy have not been particularly useful in inhibiting masculinization or in effecting feminization. Cortisone is promising as an agent to suppress excessive androgen production and to allow feminization.

Cortisone may be of use in children treated before masculine social and psychologic attitudes are established and could be especially useful in children already raised as females. In children coming under care after masculine social and psychological trends are established, surgical measures to provide as nearly as possible male anatomy should be undertaken: correction of hypospadias, removal of internal female sex organs and implantation of testicular prostheses.

Case Report

H. B., Jr., was first seen in October, 1943, at the age of three and one half years. The child was referred by his family physician with a diagnosis of hypospadias and undescended testicles. The penis was abnormally short with the typical ventral curvature accompanying hypospadias. The penis and glans penis were of normal size for a child of this age. The prepuce was adherent to the glans. The ectopic urethral meatus was at the penoscrotal junction. The scrotum was undeveloped and neither testicle was palpable in the scrotum or inguinal canal. The diagnosis was hypospadias with bilateral cryptorchidism. The parents were advised that surgical correction of the hypospadias should be postponed until age twelve and that endocrine therapy should be tried before considering surgical correction of cryptorchidism.

The patient was not seen again until June, 1951, at the age of eleven years. The parents thought that there had been normal development but that the child, which had been raised as a boy, was larger and more robust than in proportion to his eleven-year-old contemporaries. Examination now revealed abundant pubic hair with male distribution of hair extending up toward the abdomen. Neither testicle was palpable in the scrotum or inguinal region. There was a well-marked ventral curvature of the penis. In August, 1951, a first stage plastic operation for correction of ventral curvature was carried out. The result of this operation appeared good and the patient was not seen again until December, 1952. The penis was well developed and straight. An inlay tube graft construction of urethra for hypospadias was carried out in June, 1954. Plastic operation was carried out for anastomosis of the proximal portion of the urethra with the distal portion in May, 1955.

The patient returned in December, 1955, at the age of fifteen years for closure of the urethrocutaneous fistula and orchidopexy. The parents now reported that the child from age seven had been larger than his class mates and had dominated them but that since age twelve he had stopped growing. He had been taller than his class mates but was now shorter. At age ten or eleven this child had developed an interest in girls and sports. At age fifteen there had been an onset of monthly hematuria of one day's duration.

On December 27, 1955, two small urethro-cutaneous fistulae were closed and a left inguinal incision was made to carry out a left orchidopexy. Examination of the left inguinal region revealed no left testicle. The incision was then lengthened upward and the retroperitoneal space at a higher level was widely opened but still no testicle was found. The peritoneal cavity was then

opened and examination revealed two ovaries, two fallopian tubes, and a uterus. The left kidney and adrenal were exposed and appeared normal. The right kidney and adrenal were palpated and felt normal. Biopsy

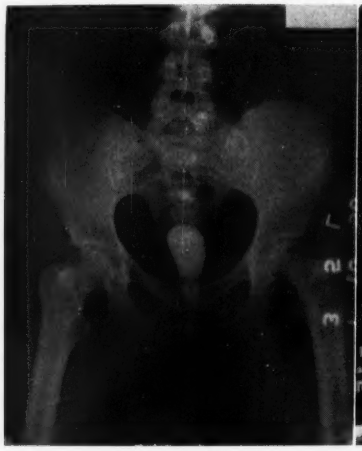

Fig. 1.

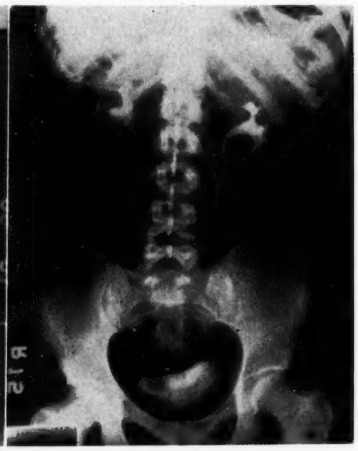

Fig. 2.

was taken from the ovarian structures. Histologic examination showed ovarion tissue on both sides. Now for the first time the correct diagnosis of female pseudohermaphroditism was made.

Review of the laboratory work of the previous admissions showed normal hemoglobin, white count, differential and urinalysis. Review of the history revealed the patient had had hormonal therapy on several occasions—the last at age twelve years—in an unsuccessful attempt to produce descent of the testicles. Postoperative determination of the urinary 17 ketosteroids was 64 mgm in twenty-four hours. Blood pressure on all admissions varied between 110 and 130/80. Post-operative x-ray examination of the left upper and lower extremities including the shoulder, elbow, wrist, hip, knee, ankle, and foot showed that all the epiphyses were closed and appeared to have been closed for some time. The radiologist stated the patient had a bone age of twenty years or more.

A cysto-urethrogram was unsuccessful because the contrast medium leaked out through the urethrocutaneous fistula. A catheter was passed through the urethra and injected with contrast medium. This radiograph showed the catheter had been inserted through the urethra into a cavity measuring about 3.5 x 9 cm. This cavity was smooth in contour and represented a vagina. Above this cavity was a collection of contrast medium which formed the characteristic shape of a uterus. The conclusion was that there was a long smooth cavity which represented a vaginal wall filled with contrast medium and a normal appearing uterine cavity attached to the upper end of the vagina (Fig. 1).

The following day excretory urograms were made which showed normal kidneys, ureters, and bladder (Fig. 2).

The patient was then seen in consultation by Dr. B. J. Kennedy of the Department of Internal Medicine, University of Minnesota Medical School. It was Dr. Kennedy's opinion that "this patient is genetically female with an adrenal genital syndrome. The patient has hyperfunctioning adrenal glands though they are within normal limits of size and I do not believe there is an adenoma of the adrenals present. As a result of the high androgen level from the hyperfunctioning adrenal, the male characteristics have predominated in that there is hirsutism, hoarseness, large clitoris, muscular development and sexual aggression towards females. He is socially adjusted as a male. The high androgen level has also stimulated his early bone growth but subsequently has resulted in complete fusion of the epiphyses. Hence, no further growth is potentially present. At the present time it would be unwise to attempt to convert this patient to the genetic female. Though this would be extremely easy to do the patient would be unable to adjust to the change of sex, and psychiatric implications would be tremendous. It would therefore seem best for the patient to have the uterus, ovaries, tubes, and vagina removed. I do not believe, however, that it is necessary to treat the adrenal status at the present time. It would be wise, however, to follow him in the future, regarding this, since a few cases of adrenal genital syndrome have a complication of partial adrenal insufficiency, though the adrenal is also producing huge amounts of a single hormone." Dr. Kennedy also added, "in an attempt to improve his masculine status I would suggest that at the time of removal of the female organs plastic testes be inserted in the labia to simulate true testicles."

The entire situation was then discussed with the patient's family and they felt that it would be impossible to have this child who had been brought up as a male now suddenly changed to a female. It was decided this patient would return at a later date for removal of the uterus, ovaries and tubes.

The patient returned in March, 1956. The urinary 17 ketosteroids were 54 mgms per twenty-four hours.

On March 25, 1956, cysto-urethroscopic examination was carried out. This showed the vaginal opening on the floor of the urethra about 2 or 3 centimeters in front of the vesical neck. The vesical neck and bladder were normal. Following the cysto-urethroscopic examination a bilateral salpingo-oöphorectomy, total abdominal hysterectomy and partial abdominal vaginectomy were carried out. The patient had an uneventful postoperative course and was discharged from the hospital on April 2, 1956. Histologic examination of tissue removed showed—uterus with atrophic endometrium, vascular ovaries, and tubes.

The last hospital admission for this patient was in April, 1957. At this time, testicular prosthesis in the form of lucite spheres were implanted in the scrotum. The urinary 17 ketosteroids on this admission were 86 as compared with 64 on the original admission. The patient has gotten along well and seems to be well fitted as a male.

Figure 3 is a full length picture of the patient as he appears today.

Discussion

Much work has been done on the treatment of patients with the adrenal genital syndrome. Adrenal surgery with resection of one adrenal and a large portion of the second adrenal has been of little benefit. The administration of estrogens to female pseudohermaphrodites may cause breast development and its withdrawal frequently leads to uterine bleeding but it does not decrease the hirsutism or check the virilization. It is now generally agreed that the use of cortisone as described by Wilkins is the best treatment in individuals with female pseudohermaphroditism.

Hodges[6] discussed the surgical and hormonal therapy of benign and malignant adrenogenic hyperfunction of the adrenal cortex and felt that hormonal therapy with cortisone was more effective than surgical extirpation of portions of the adrenal glands in controlling the adrenogenital syndrome due to benign hyperplasia of the adrenal cortex. He found that the elevated urinary 17 ketosteroids were promptly reduced toward normal levels. However, the cortisone therapy was ineffective in attempting to suppress metastasis from an adrenocortical carcinoma in a patient exhibiting the adrenogenital syndrome. He felt that the contrasting effect of cortisone on urinary 17-ketosteroid excretion in benign versus malignant hyperfunction of the adrenogenic elements of the adrenal cortex could be used as a means of differentiation.

As mentioned earlier, recent work has done much to clear up the confusing situation in regard to the adrenogenital syndrome. However, numerous cases have not been recognized early in life and have thus caused many problems in the management of this condition in later life. Frank

Fig. 3.

Hinman, Jr.,[7,8] was faced with the problem of reversing the sex of two female pseudohermaphrodites with adrenal cortical hyperplasia by plastic repair of the phallus (clitoris). A detailed study of the previous experiences of others with the course of this disease was made and the literature reviewed before these operations were carried out. Two children reported by Hinman were made boys because it was felt advisable that these children should be reared in the sex in which each would best fit physically, socially, and psychologically. The records of 149 patients reported in the

literatuure were reviewed and tabulated. Fifty-three of these patients were reported after the age of fifteen and the remainder were reported before the patient reached the age of fifteen. Of the fifty-three patients over fifteen years of age fourteen were considered to be male at birth but two were later "feminized" by clitoridectomy. The remaining thirty-nine were reared as females but four became so masculinized that it was later decided to regard them as males. Many were adjusted poorly to their environment because of their masculine physical characteristics. Hinman felt that since clitoredectomy was irreversible perhaps it had best be reserved until puberty for patients who must take suppressive doses of cortisone indefinitely. He also felt that the decision as to sex in these individuals should rest on the degree and progression or suppression of masculinization, since social and psychological patterns will follow the arbitrary environmental sex.

Prior to the use of cortisone, it was impossible to check the progressive virilization and excessive growth which occurred in cases of female pseudohermaphroditism. It is now known that cortisone will suppress the abnormal adrenal activity as shown by the decrease in the urinary 17 ketosteroids. However, when this drug is stopped the 17 ketosteroids will rise to the previously high level.

Wilkins reports that relatively small doses of cortisone are effective in suppressing the excessive secretion of adrenal androgens without causing abnormal metabolic or toxic effects. However, the minimum maintenance dose of intramuscular or oral cortisone must be determined in each case by following the urinary 17 ketosteroids and the rate of somatic growth and development. In female pseudohermaphrodites who have reached a level of somatic development comparable to that of puberty—bone age of eleven years or greater—suppression of the adrenal hyperactivity with cortisone results promptly in normal adolescent sexual development. In more mature individuals progressive virilization is checked. With proper doses of cortisone, somatic growth and development proceed normally, but excessive doses may inhibit them. Wilkins has also shown that after treatment with cortisone for one or two years its omission for two or three months permits a partial return of the adrenal hyperactivity but the 17 ketosteroids do not increase to as high a level as before treatment. Whether or not prolonged use of cortisone in female pseudohermaphrodites will be successful is impossible to say at this time. A large series of cases with long followup studies will be necessary before any unbiased statement can be made.

Summary

In summary, we have presented a case of female pseudohermaphroditism not recognized until age fifteen. This child was actually a female but had been raised a male. It was felt that from the psychological standpoint it would have been castastrophic to alter the sex. In retrospect, exploratory laparotomy carried out when patient was first seen in 1943 at the age of three and one-half years would have given the correct diagnosis and in all probability simplified many of the problems of treatment which arose when the correct diagnosis was made.

The work of Wilkins and the recent reports on sex determination by skin biopsies and by oral mucosa smears which has made an early accurate diagnosis possible—especially in new born infants whose true sex is doubtful at birth—has been discussed. The experiences of other authors in clinical management of pseudohermaphroditism has been presented. No longer is exploratory laparotomy necessary to confirm the diagnosis.

It will be of great interest to follow this "boy" and see how he fits into the pattern of social life as he grows older and also determine whether or not any adrenal insufficiency will develop in the future.

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Changes in the Skin Related to Pregnancy

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THE PREGNANT woman is subject to all the eruptions of the skin that occur in the nonpregnant woman, as well as to certain physiologic changes in the skin that are exclusive with pregnancy. Crawford and Leeper[1] reviewed the dermatologic conditions present in a series of 181 women (239 pregnancies), among whom 206 disturbances of the skin occurred. In some instances, a woman had several conditions; in others, the same diagnosis had been recorded during several pregnancies. With elimination of these duplications, there remained 182 dermatologic diagnoses. A total of 49,254 deliveries had occurred at the hospital during the same period, indicating that 0.37 per cent of these pregnant patients had dermatologic complaints.

From the best available records, it is estimated that approximately 5 per cent of patients seen in general practice have a chief complaint in the field of dermatology; this is actually 13.5 times the incidence of cutaneous eruptions recorded among the afore-mentioned pregnant patients. Thus, one might conclude that pregnant women are less susceptible to lesions of the skin than are nonpregnant women. Certainly, with reasonable conservatism, it might be said that pregnant women are no more affected by cutaneous diseases than is the general population.

The most logical way to approach this discussion is to consider first the physiologic changes manifesting themselves in the skin and mucous membranes during pregnancy and then to consider the pathologic changes of most interest during pregnancy (see table).

Physiologic Changes

Violaceous Discoloration of Vaginal Membranes.—This change is known as Chadwick's sign. The mucosa about the vaginal opening frequently takes on a dark-bluish or purplish congested appearance.

Striae Distensae.—The skin is subjected to considerable tension during pregnancy, resulting in rupture of the elastic fibers of the reticular stratum of the cutis, with the formation of depressions known as striae of pregnancy. In primiparae, these present a pinkish or slightly bluish appearance. Two varieties are observed in multiparae; some resemble those in primiparous women and are caused by the current pregnancy, while others present a glistening silvery appearance, representing previous pregnancies. These striae rarely disappear completely after delivery.

TABLE I. CHANGES IN THE SKIN RELATED TO PREGNANCY

Physiologic Changes
Violaceous discoloration of the vagina (Chadwick's sign)
Striae distensae
Enlargement and pigmentation of the breasts
Chloasma (mask of pregnancy)
Gingival proliferation
Molluscum gravidarum
Palmar erythema
Hypertrichosis
Vasomotor instability
Nevus araneus
Pathologic Changes
Herpes gestationis
Impetigo herpetiformis
Prurigo gestationis
Atopic dermatitis
Pityriasis rosea
Erythema multiforme
Lupus erythematosus
Miliaria and intertrigo
Rubella
Pyoderma faciale—acne vulgaris
Herpes simplex
Vulvitis
Tumors
Verrucae
Pigmented nevi
Hemangio-endothelioma
Neurofibromatosis

Enlargement and Pigmentation of the Breast.—Under the influence of pregnancy, pronounced changes occur in the breasts. After the second month, a delicate tracery of bluish veins appears just beneath the skin. The nipples become larger and deeply pigmented, and the areola surrounding the nipple becomes considerably broader and much more deeply pigmented, the degree of pigmenta-

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tion varying with the complexion of the woman. In blondes, the areolae and nipples become pink, whereas they become dark brown and occasionally almost black in brunettes. If the breasts greatly

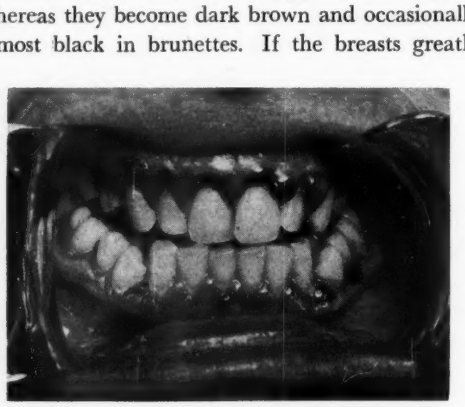

Fig. 1. Epulis gravidarum; note the dark-red, easily bleeding tumefactions.

enlarge, the skin frequently presents striations similar to those observed on the abdomen. The same degree of hyperpigmentation often is found in the linea alba (which then becomes the linea nigra), the genitals, the umbilicus and axillae, as well as around the anus and in surgical scars. All these pigmentary changes increase as pregnancy progresses and tend to disappear shortly after labor. However, the lighter shades found before pregnancy never return.[2]

Chloasma.—This condition is characterized by irregularly shaped, brown macules of various sizes that sometimes appear on the face, neck and trunk during pregnancy. When the lesions occur on the face, the condition is called the "mask of pregnancy." The exact cause is unknown. These patches nearly always disappear shortly after delivery but tend to reappear during subsequent pregnancies and may become permanent zones of pigmentation after several pregnancies.[3]

Gingival Proliferation.—Certain structures of the oral cavity appear to be adversely affected during pregnancy. Dental caries, odontitis and proliferative changes of the gingivae are among those conditions considered by some observers to be attributable to it. Full agreement, however, does not exist in this regard. The adventitious changes are acceptable as those of pregnancy, but dental caries and odontitis have been controversial issues.

The commonest adventitious change is marginal gingivitis. Generally, the lower gums are most frequently and most severely involved. This disturbance appears about the fourth month of pregnancy, usually when the mammary changes become evident. At first, the gingivae are somewhat edematous. Hyperemia soon causes more extensive changes, adding color changes to the swelling. The gum becomes progressively darker red until a dark reddish-blue tinge is attained; it bleeds easily, either spontaneously or from minor injury. This change often is termed "gingivitis gravidarum." It persists throughout pregnancy and lasts one or two months after delivery.

Under the term "pregnancy tumor" or "epulis gravidarum," a hemorrhagic proliferative change arising from the interdental gingival structures has been noted by a number of observers. This tumefaction is indistinguishable from epulis in both clinical appearance and microscopic picture. Dark-red, oval or rounded, easily bleeding tumefactions appear in pregnant women past the third month and continue to enlarge while pregnancy lasts (Fig. 1). They recede shortly after parturition.[2] These proliferative changes usually recur in subsequent pregnancies.

Molluscum Gravidarum.—Pinhead to pea-sized pedunculated small tags confined almost exclusively to the mammary region and thorax may develop during the latter months of pregnancy; they disappear partially or completely after parturition. These lesions also are seen on the sides and front of the neck. They are thought to be produced by gonadotropic hormones acting as an ectodermal stimulus. They resemble benign papillomas microscopically but have been likened to some of the pedunculated tumors found in neurofibromatosis.[2]

Palmar Erythema.—The erythema appears gradually and involves most of both palms, or it may involve the thenar and hypothenar eminences of the finger tips alone. It usually begins during the first six weeks to three months of pregnancy, reaches maximal intensity in a few weeks and then remains unchanged until after delivery. It usually recurs during succeeding pregnancies.

Hypertrichosis.—The growth of hair on the face and midline of the abdomen may increase in pregnancy.[4] This usually recedes when pregnancy

is terminated, but it is not possible to assure the patient that the problem will not persist.

Vasomotor Instability.—During pregnancy, the peripheral circulation has a tendency toward vasomotor instability. Dermographia alba or rubra occurs in about 75 per cent of patients. Increased tissue permeability is present, with occasional edema of the face and extremities. The capillary loops in the skin increase in size after the second month but return to normal shortly after the termination of pregnancy.[4]

Nevus Araneus.—Spider or stellate superficial red vascular nevi are a common accompaniment of pregnancy. They occur as superficial discrete telangiectatic lesions on the face, neck or trunk, without symptoms;[4] they consist of central elevated red dots from which fine blood vessels radiate like spokes from a wheel. They are believed to be due to increased production of estrogen during pregnancy and are frequently found in association with hepatic disease, such as cirrhosis. They occur in two thirds of white women and 11 per cent of Negro women during pregnancy and usually disappear following parturition.[5]

Pathologic Changes

Herpes Gestationis.—This condition is considered by most authorities as the only dermatologic disease peculiar to pregnancy. It may be considered synonymous with dermatitis herpetiformis in pregnancy, and it is the most severe of all the dermatoses of pregnancy. It occurs at about the fifth month of pregnancy and sometimes in the postpartum period. The disease may clear within two months after delivery, but it can recur with greater severity and at an earlier time in succeeding pregnancies.

Herpes gestationis is characterized by grouped vesicles and bullae on an erythematous urticarial base. At times only urticarial lesions are present for long periods. Lesions usually appear first in the umbilical region, accompanied by intense burning and itching; later, the groins, flanks, breasts, thighs and extensor aspects of the forearms are affected (Fig. 2). The symmetric distribution of dermatitis herpetiformis is followed. The lesions also may be found on the mucous membranes, but as a rule these surfaces are spared. The lesions may leave a small pigmented scar when they heal.[4] Eosinophilia is present in the blood and blister fluid, but the count of eosinophils rarely exceeds 10 per cent in the former.

Many miscarriages, stillbirths and monstrosities have been reported as associated with this condi-

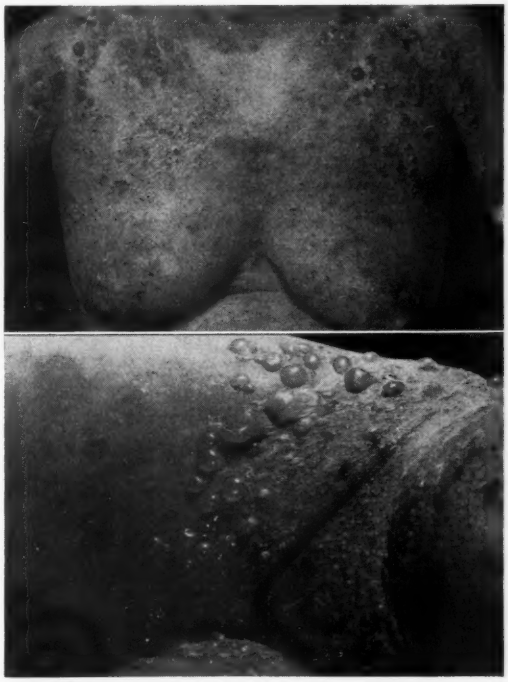

Fig. 2. Herpes gestationis of the more severe bullous form.

tion. Keaty and co-workers[6] reported on ten patients with herpes gestationis who were seen in the early stages of the disease when the symptoms were those of localized or generalized pruritus. In twenty previous pregnancies in this group, there had been a 30 per cent fetal mortality and one premature infant, and the dermatosis had appeared in each of these previous pregnancies. Of these ten patients, five had moderate to severe edema of the ankles and four had albuminuria. Persistent headache, hematuria and hypertension appeared in three. The blood levels of chorionic gonadotropin were abnormally high in seven patients, averaging 3125 rat units per 100 ml. (normal is 500 to 750 units). Since an excess of chorionic gonadotropin in the later stages of pregnancy is associated with decreased production of progesterone, substitution therapy with progesterone was used; doses of 100 mg. were given intramuscularly each day. All ten pregnancies termi-

nated in living normal infants. In our experience, use of sulfapyridine (enteric coated) or cortisone, if required, adequately controls the eruption, with safety to mother and child.

Impetigo Herpetiformis.—This is a serious disease that usually occurs in pregnant women or in the puerperal period. However, it has occurred in nonpregnant women and in men. Some clinicians have stated that this entity does not exist. The eruptive manifestations usually begin in the groin, or on the inner surface of the thighs, about the umbilicus, over the breasts and in the axillae. From these regions, the eruption spreads over other cutaneous surfaces. The early lesions are pinhead-sized (rarely larger) pustules grouped on an erythematous base. The pustules are opaque or greenish yellow and soon become covered with a dirty brown crust, beneath which the epidermis is re-formed; sometimes the surface remains red and infiltrated, and it exudes serum. The process extends by the development of new pustules in a circinate manner about the original patch. Several rings thus may be formed. By coalescence of these peripherally spreading rings from different foci, large portions or the entire cutaneous surface may become affected. After some months, when the eruption has become extensive, the skin is swollen, covered with crusts, and presents excoriated and fissured regions with irregularly disseminated circles of pustules. The mucous membranes of the mouth and throat and occasionally the esophagus participate in the process. Well-defined grayish patches with depressed centers are seen, together with erosions, which mark the site of previous pustules. Constitutional symptoms are always present and, as the disease progresses, may become grave. Fever may be continuous or intermittent. Chills and high temperatures mark each new extension of the disease. Vomiting, diarrhea and delirium occur. Bacteriologic examination of the cutaneous lesions and the blood usually gives normal results.

From 1931 through 1951, a total of fifty-six cases of this disease were reported in the literature. Of these patients, twenty-four had typical hypoparathyroidism.[7] The disease, as a rule, does not lead to abortion or premature labor and has no effect on the fetus.

Impetigo herpetiformis had a mortality rate of 75 per cent before the advent of antibiotics. The elimination of secondary infection through the use of antibiotic agents has made death due to this condition rare.

Prurigo Gestationis.—This is a generalized neurodermatitis seen during pregnancy. It has been considered as a form of atopic dermatitis by some authors. It produces generalized pruritus and becomes fully developed in the latter months of pregnancy. It is characterized by discrete pinhead to lentil-sized, severely crusted papules with an adherent bloody crust, the scratch papule. The lesions are fairly close together, depending on the duration and severity of the eruption. Characteristically, they are confined to the extensor surfaces of the arms, forearms, hands, thighs, legs and feet; when the disease is severe, the shoulders, scapular regions and thorax also are affected. The onset is gradual and the condition persists to parturition, when it promptly disappears, leaving small pigmented scars.[4] Vesicles and bullae never occur as they do in herpes gestationis. This disease does not lead to abortion or premature labor and has no effect on the fetus.

Atopic Dermatitis.—This is a characteristic form of dermatitis that differs from the purely local type in that an associated constitutional involvement, particularly of the nervous system, and also a high degree of hypersensitivity to proteins are present. Manifestations of allergy, such as hay fever, asthma, rhinitis and urticaria, often are associated; furthermore, it presents hereditary aspects in that various signs of allergy may be found in the immediate family.

This disease is characterized by a group of cutaneous symptoms, chief of which are those of lichenification, which is found most commonly on the flexor aspects of the cubital and popliteal spaces, and the sides and back of the neck. These symptoms are supplemented during acute exacerbations by other characteristic symptoms of eczema, including erythema, edema, weeping, excoriations, fissuring and crusting, together with itching, which is often intense.

This is one of the conditions that is definitely aggravated in a large percentage of cases by pregnancy. Statistics in the literature vary widely, but all authorities are in agreement that aggravation does occur and that delivery usually brings about rapid improvement. A neurogenic or neuropsy-

chiatric factor often is involved. Patients who have atopic dermatitis are usually intelligent and have driving personalities, tending to do more and to drive themselves harder than the average person does. The physical and mental exhaustion in such patients frequently aggravates the dermatitis.[8]

Pityriasis Rosea.—Hill[4] stated that this condition is more common during pregnancy than it is at other times. This impression is upheld by other authorities, although statistics are not available. It is an acute, self-limited eruptive disease that is characterized by superficial scaling patches of varying size, usually round, oval or circinate in outline, having a pale-red hue, with often a fawn-colored center, and situated chiefly on the trunk. The primary lesion often may be recognized as the largest, most conspicuous, and most brilliant in hue of all the patches. Instead of being raised, the lesion may be either on a level with the general surface or slightly depressed. The patches are dry and covered with rather adherent scales. The long axis of the lesion usually corresponds with the lines of cleavage of the skin (Fig. 3).

The causes of this disease are obscure. It is commoner in the spring and autumn than it is in the other seasons. It may be unusually prevalent during a few weeks in a given locality. This, coupled with the fact that two members of the same family occasionally are affected, lends strength to the theory that it may be mildly infective. It is generally a self-limiting disease in which the duration varies greatly in different cases.[8]

Erythema Multiforme.—This condition may occur at any stage of pregnancy or in the early puerperium, and it may disappear only to recur with subsequent pregnancies. It is characterized by intense burning and itching and fever, followed by urticarial patches of irregular size and shape. The extensor aspects of the limbs are usually affected, as is the oral mucosa. In addition to the urticarial lesions, macules, vesicles, bullae, pustules and zones of erythema are also frequently present. The characteristic lesion is the herpes iris; this variety of lesion prompted the adjective "multiforme." The condition is usually self-limited in pregnancy.[8] A relationship of this reaction to herpes simplex has become more prominent in recent years.

Lupus Erythematosus.—This condition is classified into four types: chronic localized discoid, chronic disseminated discoid, subacute disseminated and acute disseminated forms.

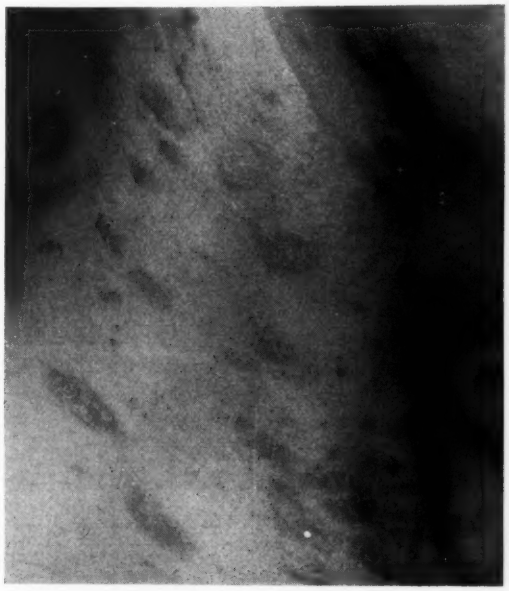

Fig. 3. Typical lesions of pityriasis rosea on the neck of a pregnant woman.

It is largely a disease of females, the maximal incidence occurring during the childbearing period. In spite of this, the number of cases complicating pregnancy is relatively small. Survey of the literature reveals that acute disseminated lupus erythematosus had a disastrous effect on the fetus or newborn child in approximately 30 per cent of the cases studied. In the acute stage, approximately 45 per cent of the patients with this disease became worse or died during pregnancy. In the subacute type associated with pregnancy, no constant effect was noted on the lupus erythematosus; however, 46 per cent of these patients aborted. In chronic discoid lupus erythematosus associated with pregnancy, practically no ill effects on the pregnant patient were noted.

The question then arises as to whether a patient who has lupus erythematosus should be advised against pregnancy. If the disease is subacute or chronic, the mother usually will go through pregnancy uneventfully, although the prognosis for the fetus is relatively poor in the subacute disseminated stage, as already noted. In the acute dis-

seminated type, because of the seriousness of the disease, it is doubtful if the risk for the mother or the child is advisable. Wellborn and Warden[9] suggested that therapeutic abortion could be justifiable in the systemic form of the disease in which myocarditis, severe renal involvement or psychosis is present.

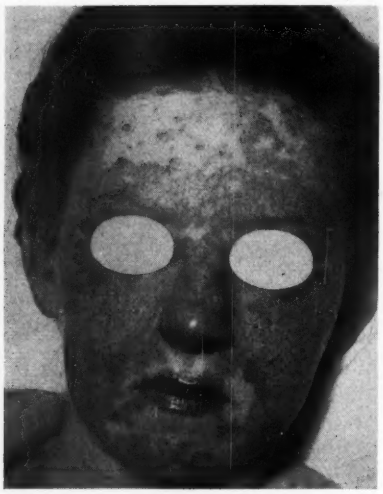

Fig. 4. Typical facies in acute systemic lupus erythematosus.

In the discoid variety of lupus erythematosus, the early stage is manifested by one or several bean-sized, slightly elevated, reddish macules that do not entirely fade under pressure and are covered with an adherent scale. The primary lesion enlarges peripherally and is well defined in outline; its color varies with the acuteness and type of the disease from rosy pink to deep purple. The shape is usually circular or oval. The border is firm, red and distinctly elevated. The lesions may spread symmetrically over the nose and cheeks in a form that has been likened to the open wings of a butterfly. As the borders advance, the center not infrequently undergoes involution, becoming paler and less elevated; it may show typical scars even while the outer rim is actively progressing.

In the primary acute disseminated type, the cutaneous lesions begin as erythematous patches on the face that coalesce and cover the cheeks, nose, eyelids and ears (Fig. 4). The face is edematous and swollen, and in some cases crusting occurs early. The eruption involves the hands and may extend over other regions. On the hands, it may be erythematous, papular or purpuric; on other portions of the body, the eruption is multiform. Involvement of the finger tips is a characteristic feature. Bullae, vesicles, scaling patches, crusted lesions, hemorrhagic lesions and generalized telangiectasia have been described. When the acute disseminated type develops from the chronic discoid form, the lesions on the face become acutely inflamed and new lesions develop elsewhere.

In the subacute type of lupus erythematosus, the lesions are erythematous scaling patches of varying size. Moderate infiltration is present, and large portions of the body may be involved. However, the lesions tend to be limited to the exposed surfaces, including the V of the neck. These lesions may undergo involution without atrophy, or varying degrees of atrophy and telangiectasia may occur. The use of antimalarial drugs has revolutionized the clinical management of these patients.

Miliaria.—This rash usually occurs during the third trimester of pregnancy and is characterized by pinpoint, raised, red papules that sometimes have a vesicular top. They are discrete and occur chiefly on the abdomen, buttocks and thighs. They are considered to be due to the excessive sweating of pregnancy, with blocking of sweat ducts by hyperkeratinization. The rubbing of lanolin into the area assists in unplugging the sweat ducts.[4] This condition is prevalent in summer and in the tropics.

Intertrigo.—This eruption frequently occurs in the fold of the groin, abdominal folds and under the breasts as a glazed, red plaque. It may be complicated by fissuring and bacterial or monilial infection.[4] It is a hyperemic condition of those cutaneous and mucocutaneous surfaces which are in constant apposition and between which there are hypersecretion and retention of sweat. It is usually found in the third trimester of pregnancy.

Rubella (German Measles).—This is an acute contagious disease characterized by a macular eruption and mild constitutional symptoms. The time of incubation is variable and usually extends over a period of one to three weeks. Mild prodromal symptoms consisting of malaise, headache

and moderate fever may precede the eruption by a few hours or a day. The rash spreads rapidly and reaches its height in 24 to 48 hours, after which it begins to recede. Usually it is most pronounced on the face and neck, with the trunk and extremities exhibiting fewer lesions.

The palms and soles often share in the eruptive process. After 24 to 48 hours, the eruption undergoes involution, which is accompanied by furfuraceous desquamation and is finished by the fourth or fifth day. The posterior cervical lymph nodes are enlarged, which is of great diagnostic importance. Other lymph nodes also may be enlarged.

The serious effect of German measles on the fetus *in utero* when the disease is contracted in the first trimester of pregnancy is well known. Children born of mothers who have had German measles during pregnancy have demonstrated congenital cataracts, deaf-mutism, congenital dental abnormalities, mental defectiveness, glaucoma, microcephaly, harelip, cleft palate and rudimentary ears. However, fetal deformities may be encountered in other diseases, such as mumps, herpes zoster, scarlet fever, varicella, influenza, hepatitis and poliomyelitis, most of which are viral in nature, as is rubella. Rubella is most likely to be confused with measles and scarlatina. The rash is essentially the same in rubella as in measles, but rubella is distinguished by a more variable period of incubation, a shorter period of invasion, less severe catarrhal symptoms and, especially, by more pronounced involvement of lymph nodes. Scarlatina is marked by severe general symptoms and signs, including fever, nausea, vomiting, headache and leukocytosis.

Pyoderma Faciale-Acne Vulgaris.—This condition is frequently produced or aggravated during pregnancy. Comedones, papules and pustules are formed. The shoulders and back are involved most frequently. The papules usually become much larger than they are in the nonpregnant state and are hard and reddish blue. The flare-up usually begins at about the third month.

Herpes Simplex.—This is an acute eruptive disorder characterized by the appearance of grouped vesicles on a mildly inflammatory base, accompanied by sensations of heat and burning, and usually occurring about the face and genitalia. It is more common during pregnancy than at other times and tends to recur during individual pregnancies and at subsequent pregnancies. It is a simple disease, usually completing its evolution within one week. The lesions occur most commonly about the lips and nose, appearing less frequently on other portions of the face. During pregnancy, they frequently occur in the genital region, on the hood of the clitoris, the labia minora and the inner surface of the labia majora or adjacent surfaces. The lesions here are preceded by itching and the sensation of heat and, rarely, by pain, which is followed by the appearance of one or several pinhead-sized vesicles situated on a hyperemic base. Considerable edema of the prepuce or labia minora may result. The disease occurs as the result of irritation or inflammation of the peripheral nerves induced by various agents. This disease is transmissible by contact, and the husband is frequently infected. Herpes simplex is a self-limited disorder and, except for recurrence, is not serious.[8]

Vulvitis.—Two such conditions stand out as important during pregnancy. These are moniliasis and trichomoniasis.

Moniliasis.—The first symptoms in moniliasis are itching, burning and smarting of the lower part of the vagina and the vulva. Inflammatory changes occur in the vagina, and intertriginous lesions are found between the buttocks and over the anterior portion of the crural folds. These lesions consist of a thin overhanging fringe of somewhat lacerated whitish epidermis forming polycyclic borders about pink moist areas. Excoriations occur later and, as a result of scratching and other trauma, dry lichenified zones replace the more superficial lesions. The mucous membrane between the labia and clitoris becomes thickened and white. Fissures and whitened areas also occur about the anus.[2]

Trichomoniasis.—This condition also becomes exacerbated during pregnancy. All of its symptoms, including the characteristic itching and burning, become exaggerated. The presence of various-sized, strawberry-red, granular lesions on the inner surface of the labia minora should make one suspicious of the presence of this infection.[2]

Tumors.—

Verrucae.—Warts frequently proliferate and increase in numbers during pregnancy, most often

during or after the second trimester. This applies also to venereal warts, which can be excited by the more profuse discharge about the vulva producing a more alkaline skin flora that is conducive to the proliferation of these lesions (Fig. 5).

Fig. 5. Verrucae (condyloma acuminatum).

Pigmented Nevi. — During pregnancy, small pigmented moles are likely to appear. Usually they are flat and are brown or dark, ordinarily being of the simple innocuous variety. However, if any flat, pigmented, brown mole, especially one situated about the toes, fingers, or genital regions, shows signs of increasing pigmentation, ulceration or crusting, increase in size or the presence of satellite lesions, suspicion of malignancy may be entertained, because pregnancy is a stimulus to melanocarcinoma.

Hemangio-endotheliomas. — Pre-existing lesions may enlarge or these benign tumors may occur for the first time during pregnancy. They commonly appear as single, red, vascular, warty growths, pinhead to pea-sized, freely movable on the underlying tissues, and with a nevoid dilation of the surrounding veins. The sites of predilection are the middle vertical third of the face, about the eyes and, less frequently, on the breasts and umbilical region. Histologically, these lesions are simple nevi and rarely become malignant, regressing spontaneously after parturition.[4] They also may be found on the external genitalia, and may grow to enormous size. Although rarely malignant, they are considered so when they metastasize.

Neurofibromatosis. — Pregnancy commonly induces an intensified growth of neurofibromatous tumors, with an increase of pigmentation and the development of pain and tenderness in some nodules.[2] This condition often becomes evident for the first time during pregnancy.

Summary and Conclusions

Many physiologic changes occur in the skin during pregnancy about which the physician need not be concerned.

Evidence indicates that not only are pregnant women no more susceptible to dermatologic lesions but they may not even be as susceptible as are nonpregnant women, or men.

The treatment of all dermatologic lesions associated with pregnancy is similar to that in the nongravid female.

Only in herpes gestationis, acute and subacute lupus erythematosus, and rubella need the physician be especially concerned about the mother and the fetus.

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Physical Rehabilitation as Related to Industrial Compensation

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Physical rehabilitation consists of conserving and exploiting the physical capacity remaining to the patient. It starts with the first care given and continues practically indefinitely. Dr. Knapp discusses both some general principles and some specific procedures.

REHABILITATION has been defined as "the restoration of the individual to the highest physical, mental, social and economic level of which he is capable." This definition is an extremely broad one; and as such, includes all of the patient's care from the time of the injury or illness until he returns to employment or becomes a permanent charge upon the community.

It has been stated that the stretcher-bearer is the first member of the rehabilitation team. This is true in the general sense because the method of transfer of the patient from the point of injury to the stretcher may help to determine the end result that will be obtained many months later. For example, clumsy or inexpert handling of a patient with a fracture of the spine may convert a relatively simple case, where the involvement is limited to the bone and recovery can be expected within a few months, into a spinal cord lesion with paralysis below the point of injury which requires long hospitalization with great likelihood that recovery will never be complete.

Following the patient's admission to the hospital a great number of people will participate in his care. These include doctors in various specialties, nurses, laboratory and x-ray technicians, physical and occupational therapists, social workers, psychologists, speech therapists, vocational counselors, teachers, engineers, brace-makers, artificial limb manufacturers and many others depending upon the type of disability presented by the patient.

Each person who participates in the rehabilitation of the patient has his own definition for rehabilitation, however. To the doctor and others concerned with medical care, it is primarily the restoration of the patient to his greatest physical capacity; in other words, his recovery from the injury or illness. To the vocational counselor, it is his restoration to employability. To the social worker it is his return to his rightful place in society. To the psychologist it is the resumption of normal mental and emotional stability. Each of these has an important position in the total rehabilitation of the patient. No one of them alone, however, provides the complete answer.

In the limited sense, physical rehabilitation relates primarily to the specific problems of recovery in those patients who are seriously injured, either by accident or disease. If we follow the course of a disabled individual, we may be able to point out the various phases of rehabilitation.

After the initial injury the patient is taken to a doctor's office or a hospital. The great majority of patients are mildly injured and can be treated satisfactorily there. The laceration can be sutured, for instance, or the fracture reduced and a cast applied and the patient may then recover from his physical disability and return to his previous employment without any further rehabilitation. These patients present no serious problems and recover maximal function through normal activity.

A somewhat more disabled person may require some specialized services, such as physical and occupational therapy. This care may be given in the doctor's office or a hospital department of physical medicine, following the fracture reduction, tendon suture, or nerve suture that has been the definitive care of the patient. A great many of these patients will then return to their previous occupations without any need for further rehabilitation procedures.

A still more disabled patient may require more

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than simple physical medicine for his restoration to the highest level of functional capacity. This may be provided either by the hospital or an outpatient center where the patient's abilities may be evaluated and proper counseling given as to the usefulness of procedures which are not medical. For instance, it may be necessary for the patient to change his occupation. This requires testing of intelligence, vocational aptitudes, vocational interests, and the ability of the patient to meet people and to compete with normal individuals in spite of his handicap. Thus a proper evaluation of his physical, mental, and emotional abilities can be made and a decision reached which will give him the best possibility of returning to full employment and of reaching a high economic level.

The most seriously disabled patient will be unable to reach his ultimate goal with this type of facility. He must enter a total rehabilitation center where in-patient care is available for his severe disability. This type of center should provide complete medical diagnosis with all specialties available, together with evaluation of the patient's ability to carry on strenuous activity without harm to himself. Muscle strength, co-ordination, and endurance testing should be included. In addition to the medical evaluation, further evaluation is performed by the paramedical personnel. Evaluation of his capabilities with regard to his mental and emotional processes is made by the psychologist. If speech problems are present, they can be evaluated by the speech therapist. Testing for vocational interests and manual dexterity should be carried out and a pre-vocational testing unit is useful to determine whether the patient actually can perform the type of work which is being planned for him. An evaluation of the social problems of the patient, his family problems and responsibilities, his economic level, his previous work experience, his home situation, the type of house and its accessibility to a disabled person, what stair climbing is necessary, the location of essential facilities, such as toilet and bedroom, may influence the decision as to the program this patient should have.

Treatment should include not only medical care for the primary problem but special attention to the complications. Joint and muscle contractures, pressure sores, urinary stones, disuse atrophy and other problems arising from prolonged disability not only receive specialized attention and treatment but measures are instituted to prevent their development or recurrence. Treatment facilities for physical, occupational, and speech therapy, gait training, strengthening exercises, stretching of contractures, development of vocational skills, training in the activities of daily living, transfer from wheel chair to bed or automobile, and, for women, instruction and practice in carrying out household activities, such as cleaning and cooking, should be available. All of these procedures should be under close and continuing medical supervision with constant change of prescription to cope with changing conditions in the patient. In other words, a complete and comprehensive evaluation program with adequate treatment for those conditions which can be overcome, but with primary emphasis on complete utilization of what the patient has left to work with, is the aim of rehabilitation.

In contrast with ordinary medical and surgical thinking where we are most interested in what is *wrong* with the patient, in rehabilitation we are concerned primarily with what is *right* with the patient. In other words, we are not so much interested in his *disability* as in his *ability*. This provides a positive approach which frequently allows us to make progress from a seemingly hopeless situation to one which offers self-care and even vocational possibilities. For instance, an engineer who contracted severe poliomyelitis which resulted in complete paralysis below the neck except for a little movement in one foot and who required twenty-four-hour residence in a respirator is supporting his family by abstracting articles of a scientific nature, thus saving the time of other engineers who would otherwise need to spend many hours reading these articles. This was done by making use of what he retained rather than what he had lost. His assets were a good brain, good training in engineering, ability to talk, ability to move his head, and ability to move one foot. All of these were utilized in his rehabilitation. His ability to move his head was made useful by constructing a device so he could turn the pages of a book by a movement of the head. At the same time, a dictaphone was connected so that the movement of his foot would turn the dictaphone on and off. In this manner he was able to abstract articles and dictate his abstracts which were later transcribed by a secretary. This was accomplished in spite of the fact that he could not even breathe by himself.

Rehabilitation Centers

Recently a great deal of interest has been aroused in the subject of rehabilitation and the establishment of rehabilitation centers. This has resulted in some interest on the part of communities and local and federal government in the establishment of these centers. The federal government supplies funds for rehabilitation which are available to local communities on a percentage matching basis. This, of course, is fundamentally a good thing. However, it has resulted in some problems that may do harm to the field of rehabilitation eventually.

Americans are so constituted that when they see an available dollar they want to grab it. Therefore, many hospital administrators planning new facilities have reached for the rehabilitation dollar without much thought as to how this rehabilitation center is going to function. This creates problems. Furthermore, this term "rehabilitation" seems to be required in the title of the service. Therefore, many strange and wonderful things are masquerading under the term "rehabilitation center," some of them not even remotely concerned with rehabilitation.

In general, there are four types of rehabilitation facilities which may be grouped together in various combinations. First, the center may be associated with a general hospital. Second, it may be separate from any hospital facility. Third, it may be strictly an out-patient facility. Fourth, it may be an in-patient facility. There are advantages and disadvantages inherent in each of these types of centers. When the center is associated with a general hospital it has the advantage that other types of general medical and surgical facilities are close at hand and easily obtainable. These include such things as x-ray, operating rooms, laboratory facilities, et cetera. One serious disadvantage is that most hospitals are desperately seeking new beds and frequently the rehabilitation center is looked upon covetously by the other services so that eventually the acute services overflow into the chronic center and it recedes or disappears. The separate center has the advantage that it can maintain its autonomy and there is no fear of its being "gobbled up" by other services. However, it has the disadvantage that it must provide x-ray and laboratory facilities. This can be overcome since these can be installed in the center itself. However, operating room facilities are not usually practical in a rehabilitation center, so this service must be purchased from available hospitals in the vicinity. This is not difficult, however, and does not constitute a real disadvantage. A strictly out-patient facility, in my opinion, does not qualify as a rehabilitation center, since the type of patient which it can handle must be ambulatory or, at least transportable, and therefore is the milder type of patient. An in-patient facility does deserve the title of "rehabilitation center" since it can handle any type of patient, severe or mild, as occasion demands. However, the best combination is an in-patient facility with an out-patient department, thus all phases of patient care can be carried on.

From the administrative point of view, most centers are run according to what is known as "the team concept." This concept means that all of those who participate in the care of the patient are on the team and they all are important, each has his own function and his own part to perform in the care of the patient. But they should all work together for the benefit of the patient. This team consists of numerous parts—the medical side of it usually includes internal medicine, pediatrics where children are treated, physical medicine, orthopedics, neurology, urology, ophthalmology, otolaryngology, psychiatry, general surgery, plastic surgery, and any other medical specialty that may be needed for patient care, depending upon the orientation of the center. Some of these will be full-time and some will be part-time, the amount of time contributed being dependent on the type of patient treated in relation to the services available. In addition to the medical members of the team there are paramedical members. Among these are the nurse, the physical therapist, the occupational therapist, the speech therapist, the psychologist, the social worker, the vocational counselor, the adaptive equipment engineer, the prosthetist, the brace-maker, and any other personnel that may be concerned with the care or evaluation of the patient.

At the Kenny Institute we feel that one of the most important members of the medical team is the referring physician, since he has information available from before the time the patient was admitted and will be carrying on the after-care of the patient when he goes home from the center. Thus he can contribute to us his knowledge of the previous care of the patient and we can contribute to him a knowledge of what is being done and the philosophy of rehabilitation

so that he can carry on the follow-up more intelligently.

We spend the first week primarily in evaluation of the patient and he is evaluated from all angles —both medical and paramedical. It is not always possible to make an accurate evaluation in that time but in most instances we have found it is possible. When this is completed we have an evaluation conference, at which time each person who has been involved in the examination of the patient presents his findings and recommendations. Then, co-operatively, we try to make a decision as to what goals may be realistic for this patient. The methods for attaining these goals are outlined and adequate prescriptions given, not only medical, but also social and vocational. We try to make these goals practical and not too remote because most patients have difficulty in accepting a remote goal. For instance, we may have in mind eventual placement in a job which will require ambulation, but we may have to approach it in stages; at first, using wheel chair transportation as the practical mode of getting from place to place, and using ambulation only for exercise. At a later date, ambulation only crutches and braces may be practical for complete locomotion and the wheel chair may then be discarded.

When the physical rehabilitation of the patient has been completed and we are ready to return the patient to employment, difficulties are frequently encountered. The employer may be reluctant to hire a handicapped person because of fear that he may incur further injury because of his handicap. This fear has no foundation statistically because studies of this factor have shown that in general these workers have less tendency to injury and are usually so well motivated that absences from all causes are less than in the normal person. Some of this resistance to employment of the handicapped may come from insurance companies. At least the employer often claims this is so.

Sometimes the patient cannot be returned to competitive employment directly because of physical, mental or emotional factors within himself. His endurance may not be adequate for an eight-hour day of hard work or he may have lost confidence in his capabilities because of prolonged illness. In such instances a sheltered workshop is valuable.

Sheltered Workshops

Sheltered workshops are ordinarily of two types —the transitional and the terminal. In the transitional sheltered workshop the patient is instructed in an occupation or carries on a certain kind of work under conditions which are within his capabilities so that he may have his strength and confidence restored and can later return to competitive employment. The terminal sheltered workshop is used for those individuals who cannot compete in industry and must be employed permanently in a facility which offers some protection from the necessity of competition. Such sheltered workshops often are established to cope with certain types of disability; for instance, societies for the blind and hard of hearing have special sheltered workshops. They do not always serve to give the individual sufficient income to carry on his family responsibilities but frequently they do help to restore his sense of self-respect and self-importance because he can contribute at least partially to the financial needs of himself and his family.

I feel that it is important for the vocational counselor not only to advise the client as to his capabilities and arrange for adequate training, but also to follow him until he is actually employed in a manner that is satisfactory both to the employee and the employer.

Follow-up on these patients from all points of view—medical, social, psychological, and vocational—is needed almost unendingly because problems may arise at any time. Many of them may be solved quickly if detected in the early stages or may be prevented by adequate follow-up.

The types of disabilities that may need extensive rehabilitation procedures cannot easily be enumerated because we are treating not so much the disease or injury as the results of the disease or injury. Thus, many patients who obviously cannot be improved medically may still receive benefit from rehabilitation. The exact medical diagnosis—fracture, tendon laceration, arthritis, et cetera—is thus not as important as the factors producing disability—contracture, weakness, pain, deformity, and so forth.

A few of the conditions which more commonly require physical rehabilitation are discussed here.

Conditions Commonly Requiring Rehabilitation

Fractures.—Those fractures which are likely to produce contractures, fibrosis, or weakness, and

those requiring prolonged immobilization (especially in the presence of prolonged swelling) require treatment directed toward the prevention or correction of these factors. In general, these are: severely comminuted or compound fractures; those with delayed union, non-union, or mal-union; fractures into or near joints; and those accompanied by nerve or tendon injuries.

Especially important is the patient suffering from a fracture of the spine with spinal cord injury and resultant paralysis. If this occurs in the neck, the victim has paralysis of the lower extremities and trunk and of portions of the upper extremities depending upon the level of the lesion. Usually hands and triceps are paralyzed. This patient is usually not ambulatory, requires a special wheel chair and adaptive devices or surgical procedures must be used to make the hands functional. When the injury occurs in the dorsal or lumbar area the patient has a paraplegia resulting in paralysis of the lower extremities and trunk. However, he still has adequate upper extremity function and many of these patients can be made ambulatory on crutches and braces but most of them have residual urinary tract problems difficult to solve. The lower the level of injury, the more functional the patient will be.

Skull fractures may result in brain damage. In this case the results depend upon the severity and location of the injury. If the motor area on one side is involved, the symptoms may be similar to a "stroke" which will be discussed later.

Dislocations.—Dislocations present the same problems as fractures. Nerve injuries may accompany them, particularly in the shoulder joint.

Amputations.—Many amputees require treatment in the rehabilitation center. The objectives of this treatment are to prevent or correct contractures, to develop muscle strength, to prescribe a proper prosthesis and see that a satisfactory fit is obtained and to train the patient in the use of the prosthesis.

Patients with upper extremity amputations should have a complete evaluation of the factors of employment before prescription of the prosthesis and they usually require long periods of training to develop skill in the use of the prosthesis. This is often done best in the occupational therapy department.

Persons with lower extremity amputations should receive special attention to the possibility of hip flexion contractures. If these are present, even though very mild, the patient may assume that his prosthesis does not fit and he will discard it, going back to crutches or wheel chair (possibly becoming non-functional) whereas function would have been possible if the contracture had been prevented in the early stages of the amputation or had it been treated adequately in the later stages. This requires prolonged treatment in order to be successful.

Gait training should be started as early as possible and continued until the patient has full confidence in his ability to handle the prosthesis under all conditions.

Multiple amputations increase the problems but many multiple amputees can be returned to useful function and employment.

Tendon Lacerations.—Tendon lacerations are notoriously difficult problems, especially those in the hand. We have two conflicting objectives here. We must obtain solid healing of the cut ends and yet prevent adhesions to the surrounding structures which would limit motion. Treatment should be begun as soon as the skin wound is healed. It requires skill and patience to obtain the best results.

Peripheral Nerve Injuries.—In peripheral nerve injuries it is important to realize that regeneration proceeds very slowly. Degeneration continues for about a month and then regeneration begins which proceeds at the rate of about an inch a month. Electrical diagnosis often helps in determining the depth of degeneration. Interrupted galvanic stimulation is useful in maintaining muscle contractility and preventing fibrosis during the period of regeneration which may last as long as two years.

Back Injuries.—Back injuries constitute the greatest bug-a-boo of compensation medicine. Most of them can be treated successfully in a general hospital or the doctor's office and the patient restored to working capacity with a minimal amount of physical treatment. However, some of the most severe cases will require long periods of rehabilitation, and many of these persons cannot be rehabilitated.

During the acute phase the physical measures

are directed toward relief of pain and muscle spasm. Heat and massage, traction, and the Williams position are useful for this purpose. Braces should be avoided if possible because the patient often tends to depend too much upon the brace. This is followed by gradually increasing exercise and gradual resumption of activities. Accurate diagnosis of the causative factors is extremely important but often extremely difficult.

In the chronic stage, again, careful evaluation of the factors that are prolonging the disability is necessary and treatment is directed toward these factors. Surgery is occasionally necessary and is effective against sciatic pain but often does not relieve backache which is frequently due to muscle shortening and fibrosis.

Psychosomatic problems are often encountered. In those patients who have psychosomatic overlay on their back injury, and are disabled more by the mental reaction to illness than by the illness itself, the psychologic impact of a complete evaluation by many individuals, who then arrive at a type of treatment which seems logical to the patient, may restore him to functional capacity. We have had this happen in numerous instances.

Hysterical Paralysis.—Patients with hysterical paralysis may be benefited in the same way.

Poliomyelitis.—Poliomyelitis is a disease resulting in multiple types of paralysis which often requires very intensive rehabilitation in order to get the patient back to work or to self-care. It constitutes a large part of our patient load.

Hemiplegia.—Hemiplegia, the ordinary stroke, presents many problems of a severe nature. If the hemiplegia is on the right side of the body the patient is likely to have speech difficulties in addition to paralysis. These depend in severity on the amount of damage that has occurred in the brain. Some of these patients can be improved or restored to good functional level by speech therapy. Some others, especially those who had severe brain damage, cannot be restored to useful levels of speech. Occasionally, a patient will have only the speech area knocked out while retaining his function of arms and legs. These patients, however, usually have good reasoning powers and may be able to carry on in a vocational situation.

Persons experiencing left hemiplegia are not usually disabled as to speech but do have certain problems related to mathematics and spatial discrimination which may be even more disabling than a speech problem. Such patients tend to disregard things on the left side of them and often do not realize that the left arm and leg are functioning. They tend to bump into objects to their left. They may make mistakes in calculation and mistakes in judgment but do not realize such mistakes have been made.

Arthritis.—Arthritis is a disabling disease, certain phases of which may respond to rehabilitation procedures. The actual course of the disease may not be altered by any medical or physical method. However, the functional ability of the patient may be altered greatly by adequate physical treatment; particularly in those instances where the disease has run its course and is no longer active but the patient is left with joint ankylosis, limitation of motion, and deformity. Plans can be made so that the patient will return to employment with the aid of devices to help ambulation or to help function of the upper extremities.

Certain problems related to other diseases such as muscular dystrophy, multiple sclerosis, amyotonia congenita, and many others may be benefited by rehabilitation.

Conclusion

The philosophy of rehabilitation is fundamentally the use of those capabilities remaining to the patient following severe disease or injury to restore him to the highest physical, mental, social and economic level of which he is capable.

DIABETES DEATH RATE

Does marital status play a role in diabetes? Prior to the age of forty-five the death rate from diabetes is higher for single women than for married women. For example, between the ages of thirty-five and forty-four the death rate is approximately 65 per cent higher for single women. However, after the age of forty-five the death rate for married women exceeds that for single women. Among men, the death rate from diabetes is greater for the unmarried until the age of seventy.—*Patterns of Disease.*

Management of Acute Injuries of the Head

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This modern age of speed brings with it an increasing toll in severe head injuries. Ideally, such injuries are managed by a neurosurgeon, but one is not always available. Thus, all physicians should know something about the treatment of those acute cranial emergencies that cannot wait for the neurosurgeon. This article briefly discusses the management of a few of these emergency situations, with emphasis on acute subdural and acute extradural hemorrhage.

AS THE population of this country increases and the inhabitants find themselves moving ever more rapidly in their environment, they encounter increasing numbers of problems, one of which is acute injury to the head. The commonest source of serious head injury is automobile accidents. Damage to the brain and spinal cord causes 70 per cent of the deaths resulting from automobile accidents. About 70 per cent of deaths from head injuries take place in the first twenty-four hours.[1] Associated injuries frequently may take precedence over the head injury. Therefore, the proper care of the severely injured patient is best handled as a team effort involving several surgical specialties. However, the cranial trauma frequently takes precedence over other less devastating injuries.

Ideally, the head injury should be treated by a neurosurgeon but, unfortunately, one is not always available. Consequently, some head injuries must be treated by other physicians. Therefore, I believe that physicians are obligated to acquaint themselves with those head injuries which require immediate lifesaving procedures.

Two conditions are particularly important in this regard. They are acute subdural hemorrhage occurring in newborns or extremely young babies and acute extradural hemorrhage occurring in adolescents and older persons. These situations frequently require immediate definitive surgical action. Some cranial emergencies require other types of immediate action to save lives, such as tracheotomy.

Classification of Head Injuries

It is important to this discussion to present a classification of head injuries that is clinically appropriate. It is convenient to divide them into three types, namely mild, overwhelming and "indecisive." Lacerations of the scalp and concussion are examples of mild head injuries not requiring much treatment or concern. Overwhelming injuries include crushing types of trauma, massive intracerebral hemorrhage, massive intraventricular hemorrhage, and laceration of the midbrain or brain stem. This group includes those injuries incompatible with life and, consequently, patients so injured rarely survive long enough to see a physician.

The third group, the "indecisive" type, includes acute extradural hematoma, acute subdural hematoma, chronic subdural hygroma, chronic subdural hematoma, depressed skull fracture, basal skull fracture, traumatic cerebral edema, and some instances of brain laceration and hemorrhage. These injuries can be effectively treated in many instances, with the preserving of many lives. Most of these patients will survive long enough after the initial trauma to reach a neurosurgeon.

Pathologic and Physiologic Aspects of Head Injuries

The pathologic aspects of injury to the brain may be discussed briefly under the categories of concussion, contusion, laceration, thrombosis and edema. One might consider concussion as a temporary physiologic disruption of brain function without anatomic evidences of disruption. It is described as a consistent reduction of activity in the reticular substance of the midbrain or paralysis of the reticular activating system.[2] Contusion

Read at the Clinical Reviews sponsored by the Mayo Clinic and the Mayo Foundation, Rochester, Minnesota, April 14 to 16, 1958.

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might be considered as "bruising" of the brain without gross anatomic interruption of brain tissue. Laceration of the brain is actual anatomic interruption of the tissue. Thrombosis and edema

dural hematoma and subdural hygroma are rarely emergency situations. Patients with such lesions should be referred to the neurosurgeon. The presence of such lesions is recognized by progres-

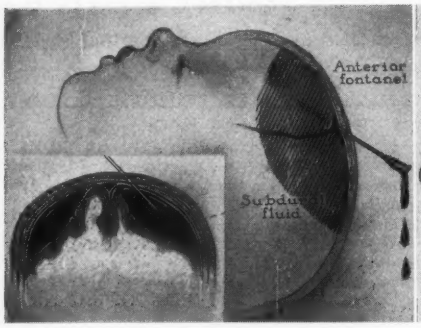

Fig. 1. Drainage of acute subdural hemorrhage in an infant by needle puncture through the anterior fontanel.

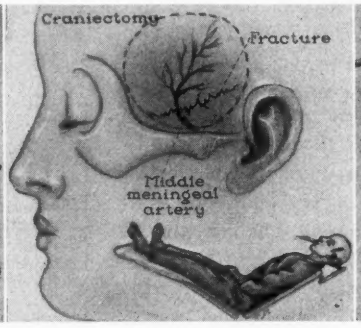

Fig. 2. Temporal craniectomy for fractured temporal bone that has lacerated middle meningeal artery and caused acute extradural bleeding.

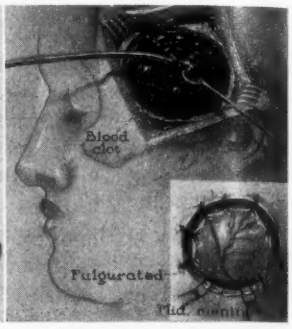

Fig. 3. Evacuation of blood clot and coagulation of middle meningeal artery in acute extradural bleeding.

are the result of structural changes in the blood supply and drainage of the brain, with physiochemical alterations in the "blood-brain barrier" and cellular structures.

Physiologic changes are manifested by focal and generalized alterations in brain function. If a motor area is lacerated, focal paralysis results. If generalized edema occurs, it is manifested by increased intracranial pressure and resultant slowing of the pulse, increase of blood pressure and deterioration of consciousness. This clinical picture does not identify or localize the lesion but only signifies increasing intracranial pressure. Both localized and generalized phenomena may be seen simultaneously. Surgical intervention usually is indicated when there are evidences of progression of focal signs or evidences of increasing intracranial pressure or evidences of both.

Treatment of Indecisive Head Injuries

In considering the indecisive group of head injuries, I shall mention briefly those usually treated by the neurosurgeon. The situations that may be encountered by physicians who are not neurosurgeons will be outlined in more detail.

Acute subdural hematoma in adults usually is associated with injuries to bone and brain and is rarely observed in a "pure form" requiring immediate exploration. When it does necessitate emergency attention, it simulates extradural hemorrhage and is treated accordingly. Chronic subsive evidence of increasing intracranial pressure and focal signs such as progressive paralysis, focal seizures or unilateral pupillary dilatation.

Depressed skull fractures and penetrating injuries should be débrided but in this age of antibiotic therapy the emergency is not particularly acute, and the patient can be transported to the nearest available neurosurgical center. Basal skull fractures are not usually surgical emergencies but precautions should be instituted to prevent meningitis. Leakage of cerebrospinal fluid from the nose or ear may accompany such injuries. Closed head injuries that produce cerebral edema are frequently more serious in the acute phase than are the more gruesome compounded, comminuted, brain-lacerating fractures. In the former, the brain sustains a greater impact and suffers more serious damage than it does in the latter, in which the impact is dissipated by fractured bones and focal zones of lacerated brain without such truly devastating trauma to vital regions. Decompressive procedures in closed injuries occasionally are indicated. More recently, however, the tendency has been to perform tracheotomy to allow better oxygenation of these patients and, on rarer occasions, to decrease the body temperature by refrigeration to lower the metabolic rate and reduce cerebral edema. Cerebral anoxia, increased blood pressure, venous stasis, high fever and increased metabolic rate are all signs of impending disaster that is best combated by a better oxygen supply

to the brain and reduction of the basal requirements of the brain tissues.

When confronted with a head injury, most physicians can stop bleeding by the usual methods. An adequate airway is maintained if necessary by tracheotomy. If the patient is a newborn or is less than eighteen months of age and appears to be dying of intracranial bleeding, the lateral aspects of the anterior fontanel can be entered with needles, which allows one to identify acute subdural hemorrhage and relieve the pressure by the escape of blood through the needles (Fig. 1). This procedure usually can be accomplished in a moment and a life may be saved. It can be done once or twice daily if necessary until the bleeding stops. If the fluid then becomes xanthochromic, the child can be transferred to a neurosurgical center for craniotomy and removal of the inevitable membranes.

The other acute emergency that must be recognized and that might have to be treated by physicians other than neurosurgeons is acute extradural hemorrhage. Classically, an adolescent riding his bicycle falls and strikes his head, or he is hit by a car and injures his head. He is momentarily dazed, but then he gets on his bicycle and goes home. During the next hour, headache develops, he becomes generally ill and vomits, contralateral paralysis and an ipsilateral dilated pupil appear and he becomes unconscious. At this stage, the situation is a dire emergency. He is in trouble because he has fractured his temporal bone and in turn the fracture has lacerated the middle meningeal artery. This has caused extradural bleeding in the middle cranial fossa. He is drowsy and feels ill because of rapidly increasing intracranial pressure. He has contralateral paralysis because of pressure on the ipsilateral motor area. He has an ipsilateral dilated pupil because of herniation of the temporal lobe through the tentorial notch, with compression of the third cranial nerve. Surgical intervention is imperative and must be accomplished without delay. Temporal craniectomy is done (Fig. 2), with the patient prepared for bilateral exploration, as the bleeding rarely may be on both sides.[3] The blood clot is evacuated and the middle meningeal artery is coagulated, tied, clipped or packed (Fig. 3), but the pressure must be relieved immediately. The actual loss of blood is usually inconsequential. Some patients may be transported to a neurosurgeon for this treatment; if it is a matter of a 30-mile trip, the patient might be saved, but a 90-mile trip might result in death. Therefore, the recognition and treatment of this condition should be familiar at least to anyone who calls himself a surgeon. If not, preventable deaths will continue to occur.

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CYSTS OF THE SPLEEN

(Continued from Page 618)

Large cysts originating in the splenic parenchyma are symptomatic but do not cause hypersplenism. The greatest single aid in diagnosis is a roentgenologic examination. The treatment of this rare condition is splenectomy.

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Arteriography and Cardioangiography

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ARTERIOGRAPHY and cardioangiography have become accepted adjuncts in the field of roentgen diagnosis. It is the purpose of this brief paper to show that their applications are many, exclusive of the field of intracardiac anomalies. As intimated, it is a procedure which is of practical value in determining the advisability and/or feasibility of surgery, directly or indirectly associated with vascular problems.

The procedures are usually a joint project between the surgeon and radiologist. Suffice it to say, the radiologist must provide a rapid film changer and radiographic equipment capable of at least six, and possibly twelve, exposures per second. Another essential is that of a mechanical contrast injector. Manual injections are inadequate except when working with infants. Special contrast agents containing high percentages of iodine and special catheters are also necessary. Cine radiography will probably supplement the rapid film changers in the future.

Space does not permit us to discuss the techniques, but two approaches are used. Forward angiography was the most widely used approach until the more satisfactory selective angiographic techniques were developed. Forward angiography refers to the injection of a contrast agent through the antecubital vein or saphenous vein. This results in rapid dilution of the contrast with inevitable loss of detail in children and adults. It is relatively satisfactory in infants. Selective angiography refers to the insertion of a catheter directly into the vessel or cardiac chamber to be examined. As a result, the contrast delineates the segment being studied more vividly, and the extraneous vascular shadows are avoided.

The following five cases briefly demonstrate the value of the procedure in determining the necessity and/or feasibility of surgery.

From the Departments of Radiology, Mount Sinai and University of Minnesota Hospitals, Minneapolis, Minnesota.

Presented before the Minnesota Surgical Society, Mt. Sinai Hospital, Minneapolis, Minnesota, November 1, 1957.

Case Reports

Case 1.—The patient was a thirteen-month-old Indian boy born in a tuberculosis sanatorium. The child was physically underdeveloped and had exhibited respiratory distress and pallor since the age of nine months.

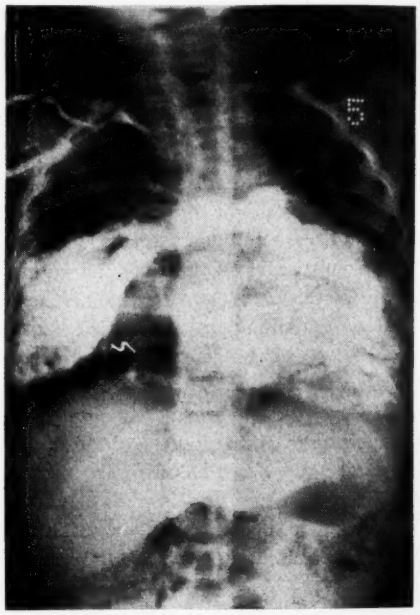

Fig. 1. *(Case 1)* Angiogram showing fill of large arteriovenous communication from large right pulmonary artery into congenital defect in right middle lobe and to a lesser extent in the right lower lobe. (Feinberg, S. B.: Roentgenographic Findings in Respiratory Problems in Infants. MINNESOTA MEDICINE, 39:285-289, May, 1956.)

On admission to the hospital, a patch of central homogeneous density with peripheral patchy densities was noted to occupy the middle lobe, as determined by radiographic examination. Some observers interpreted this as representing tuberculous pneumonia.

A suggestion of serpiginous vessels was noted and angiography was recommended in spite of the absence of bruit or polycythemia.

Angiograms (Fig. 1.) confirmed the impression of a massive arterio-venous communication of the right middle lobe as well as a smaller one in the anterior segment of the right lower lobe.

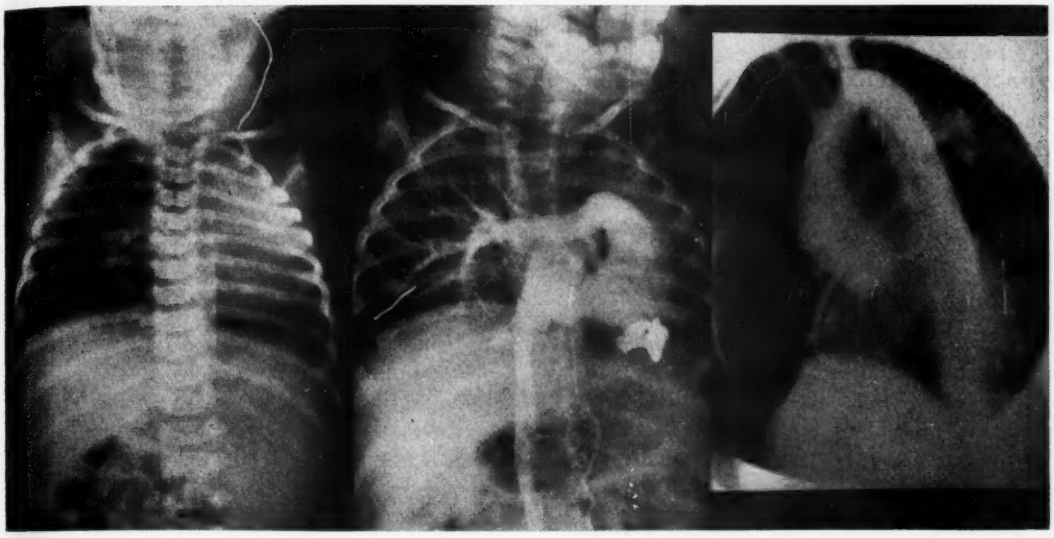

Fig. 2a. *(Case 2)* Question of atelectasis of left upper lobe with shift of heart and mediastinum to left as well as deficient vascular pattern in left lower lobe. Absence of bronchial airway suggested agenesis of left upper lobe.

Fig. 2b. *(Case 2)* Angiogram showed large but normal right pulmonary artery. On the left, an underdeveloped artery was noted going to the lower lobe, but no pulmonary artery to the upper lobe was present.

Fig. 3. *(Case 3)* Previous operative diagnosis of aortic-pulmonic window was questioned. A retrograde aortogram showed no abnormality or pulmonary artery communication. This examination shows the advantage of retrograde aortography for the study of the coronary arteries.

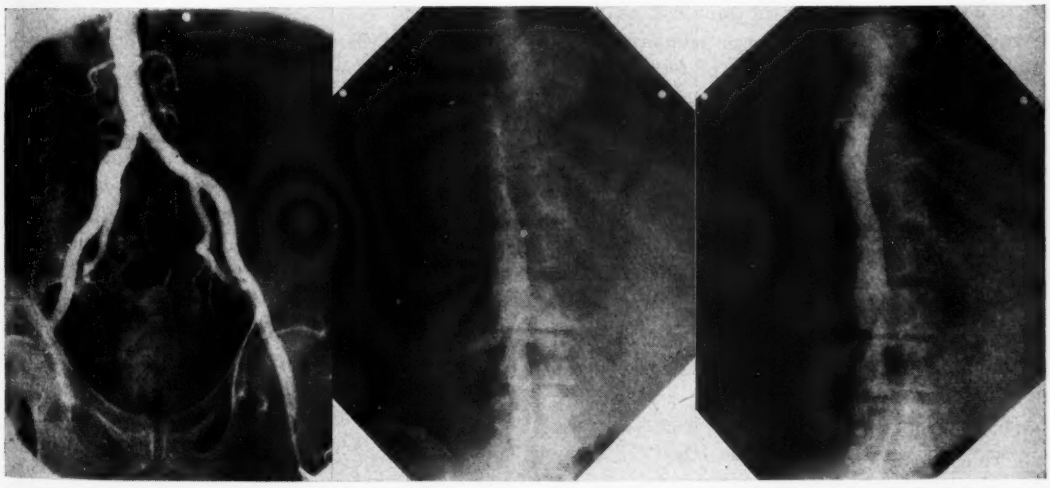

Fig. 4. *(Case 4)* A left femoral retrograde aortogram was used to avoid the dangers of percutaneous aortography. An aneurysm of the right iliac artery was demonstrated.

Figs. 5a and 5b. *(Case 5)* Inferior venacavagram using retrograde catheter to evaluate the possibility of vena cava obstruction was done. No vena cava obstruction was present.

Case 2.—The infant was nine months old when first seen. She was reported to have had pneumonia "early in life." Her radiographs showed homogeneous opacification of the left upper lobe with retraction of the lingula and compensatory emphysema of the left lower lobe. Because of the lack of air-filled bronchi and the small left pulmonary artery (Fig. 2a), agenesis of the left upper lobe was suggested.

Angiograms (Fig. 2b) showed a diminutive left pulmonary artery going to the left lower lobe with no branch going to the left upper lobe.

(Continued on Page 663)

Special Article

A Neurologist's Escape to Lapidarian Delights

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Rochester, Minnesota

A FRENCHMAN once said, "If a man has not become a gardener by the time he is forty years of age, he will most certainly lose his mind." Even less colorful epigrams to the same point have survived the centuries, and epigrams survive only because they are trenchant reminders of disregarded experience. But it seems to be a happy provision of nature to entice most of us into some kind of gardening early in childhood.

Herman Melville observed in *Moby Dick* that all men's footsteps turn instinctively toward the sea. But the sea was far removed from my home in southern Illinois, and as soon as I could walk, my footsteps turned instead toward the coalbin. There, in the lustrous soft coal and to my mother's dismay, I spent many happy hours in searching for imprints of ferns, crystals of gold and other treasures.

"Earth Has One Tale to Tell"

The results of these studies were never published, for I was still in short pants when father took us back to my native state, Wisconsin. There I discovered gravel, and soon stones were running through the holes in my pockets. I might never have learned what lay hidden from sight within those stones had good fortune not again taken up its pursuit of me. My first teacher in the lapidary art was an internist, a friend of many of you, that versatile genius, the late Charles K. Maytum. To him I owe a debt of gratitude, for presently I became a member of a fraternity that gives no examinations, requires no theses, charges no dues and is lavishly endowed. There is convincing evidence that preparations for our coming were underway some three or four billion years ago. It was of this period that Job so eloquently said, "He stretcheth out the north over the empty place and hangeth the earth upon nothing." In this monstrous kitchen minerals and mixtures of minerals that we call "rocks" came into being. And ever since, and even now on the more gentle earth we know, the forces of nature continue restlessly at work for us.

We have been warned to beware of a man without a weakness. By this criterion the collector of rocks and minerals is safe, for every stone in his neighborhood commands his attention. Or you may find him thousands of miles from home on his hands and knees, hopefully searching for a stone reputed to be hidden in the earth. To be sure, there are risks involved in such pursuits. Once, on the jade fields of Wyoming, I stood suddenly frozen by an ominous rattling sound. My eyes cautiously surveyed the ground on which I stood but could detect no source of this disturbance. Finally I ventured to move on, and when I overtook my friend, who knew the country well, and told him of my fright, he laughed and said, "There are weeds here with seed pods that rattle when the wind blows very hard, as it is doing today. These rattling pods sound just like snakes."

In Montana I came across a sign I thought was meant for trespassers:

"In frontier days the average party's demise was plumb abrupt. . . . The pioneers, being a vigorous breed, and tough as leather, were hard to kill with a 45-90 slug. . . . So when a gent was called he usually left in a cloud of smoke. . . . Because of the occupants' habit of fading out in their moccasins, this necropolis has long been known as Boothill Cemetery."

Read at the meeting of the Minnesota Society of Internal Medicine, Rochester, Minnesota, October 21, 1957.

Dr. Woltman is an Emeritus Member, Section of Neurology of the Mayo Clinic and Mayo Foundation, Rochester, Minnesota. The Mayo Foundation is a part of the Graduate School of the University of Minnesota.

AUTHOR'S NOTE: This title, being the best part of the paper, should be read last. Because the program had to go to press while the author was away, my colleague, Dr. James Eckman, contrived one of his routine but invariably brilliant "escapes."

"Beauty Provoketh Thieves Sooner Than Gold"

But the amateur lapidarist's most characteristic weakness is a growing, gnawing love for the motor of his wife's washing machine. At last this temptation overwhelms him and he steals the motor without compunction or loss of fraternal esteem. Yet all this mischief prevents worse mischief, for a man's mind, like an old board, will warp unless it is nailed down.

"Hand and Mind Can Use the Tools They Get"

Now, having gotten a stone and a motor at little or no cost, the lapidarist is ready for business. His problem is to cut the stone. The man in a shack and in the shadow of a mountain may do this with the lid of a tin can or a disk cut from an old fender. This disk, now called a "saw," is spun through a bath of mud to which an abrasive, such as silicon carbide, has been added and the stone, usually swung on a hammock or mounted on a carriage, is moved into the edge of the spinning disk which bites its way through the stone. The gentry usually buy a saw, the edge of which has been charged with diamonds. Such a saw cuts faster. Because heat is generated, a liberal supply of oil or water is used as a coolant. The water also washes away the sludge.

A cut slab of stone is rough and disappointing and calls to mind Flaubert's disconsolate general, Hanno: "Tears coursed down his face as winter rain over a ruined wall." But one may get some idea of what the stone will look like when it is polished by dipping it into water, or, if no stranger is around, the custom is to call out that capable and willing servant, the tongue.

The next step is called "sanding." This may be done by holding the stone against a grinding wheel or on a horizontally rotating disk of cast iron, called a "lap," on which an abrasive powder, usually silicon carbide, and water have been sprinkled. By manipulating the stone the worker can give it any desired shape. Scratches are successively removed by the use of fine and finer grits of abrasive. The stone is now ready for polishing.

Polishing may be done by holding the stone against a felt wheel dressed with a polishing agent, such as tin oxide and water. No sooner does the stone touch the wheel than it springs to life, translucent and radiant with color. These polishing agents often are softer than the stone, and just how they work is not known. Some electrical phenomenon may be involved.

In the shaping and polishing of smaller stones recourse is had to a device that has come down through the centuries. The fragment is cemented to the end of a stick, called a "dop." This not only assures control of the stone and prevents an opal's being shot across the room and breaking into bits, but it also forestalls a sanguine manicure. Opaque stones are commonly cut to an oval shape, the bottom flat, the top convex. This cut is called "cabochon."

Transparent stones require transmitted light to bring out color or brilliance. Hence, such stones commonly are faceted. The refractive index of the mineral determines the proper inclination of these facets, front and back, relative to the horizontal girdle of the stone. The object is to cause the light that enters the top of the stone to be reflected by the bottom, so that it will pass through the stone once more, this time from the bottom back through the top. Thus, the bottom serves as a mirror. The standard brilliant cut calls for fifty-seven facets. Accurate placement of these facets is not done freehand, but with help of some graduated and steadying device, such as a gim peg or a faceting head.

There is still another way of polishing stones in which irregularity of shape is emphasized. This is achieved by tumbling fractured stones in a revolving barrel, first with water and an abrasive, then with water and a polishing agent. The result is pleasing. Such stones are especially suitable for use in earrings and bracelets. This finish is called "baroque."

Spheres usually are cut between the ends of two pipes that are somewhat smaller in diameter than the sphere to be made or by running the stones in a race between two laps.

For purposes of microscopic study and identification, stones are sometimes ground to a powder, or sections are cut to a thickness of about 25 microns and mounted on a glass slide, much as a pathologist mounts tissue. This technic, introduced about the middle of the last century by Henry Clifton Sorby, an English geologist, complemented by the work of chemists and crystallographers, revealed the private lives of rocks and made petrology an exact science. Such preparations, when viewed with polarized light, may exhibit a remarkable display of colors. The wave

length and deflection of the light that is transmitted help to identify the mineral.

"Full Many a Gem of Purest Ray Serene"

No stone is without interest, but some stones appeal more to the eye than do others. To qualify as a gem stone, the mineral should be beautiful and it should be durable. Yet a dandelion is both of these. Obviously, this is not enough. A gem stone must also be scarce and it must be fashionable; something I have that you want, or vice versa. These features underlie a rather confusing terminology. The precious stones constitute that stately and sparkling procession: the diamond, the sapphire, the ruby and the emerald. All other gem stones are semiprecious, even though some of these may cost more than a precious stone. The Roman senator, Nonius, paid the equivalent of $800,000 for the greatest opal of his time. Occasionally a diamond with color—yellow, blue, green or red—is found. These are called "fancy stones"; they also command a fancy price.

Perhaps the most famous of these fancy stones is a diamond called the "Hope Blue." It weighs 44.5 carats, or slightly less than 9 gm., and is about an inch across. Its origin is cloaked in mystery, but it appeared in London in 1812, in company with a smaller blue diamond. It then disappeared for eighteen years, then turned up in a London pawnshop, where it was bought in 1830 by Sir Henry Thomas Hope for some $90,000. Later it adorned the favorite wife of the Sultan Abdul-Hamid. In 1911 it was purchased by Mr. Edward McLean, of Washington, D. C., for an undisclosed sum, possibly $300,000. It is now in the possession of Mr. Harry Winston, a New York jeweler, and recently it has been said that it might be acquired by the Smithsonian Institution. Earlier, two blue stones were mentioned. These are thought to have been part of a 67-carat uncut blue diamond that was brought from India in 1642 by a French traveler, Jean-Baptiste Tavernier, and later sold to Louis XIV of France. In 1792, during the French Revolution, this stone could not be found among the plundered crown jewels. Famous gems are known the world over, and the thief of any one of these would be safer with a pocket full of radium.

The common unit of weight is the metric carat. A carat is equivalent to 200 mg.; divide the carats of your wife's diamond by 5 and you have its weight in grams. A point is 1/100 carat, or 2 mg.

A mineral more familiar to us than diamond is corundum, aluminum oxide, which, because of its hardness, is used in the manufacture of grinding wheels. But, given a clear crystal of corundum with a trace of chromium, you have a ruby; add instead of chromium a trace of titanium and it becomes a blue sapphire. Rubies are always red, but corundum in any other color, be it pink, blue, green or yellow, is sapphire. In this country rubies and sapphires have been found in North Carolina and Montana. A good ruby may cost twice as much as a diamond and an emerald four times as much.

Quartz is most familiar to us in the form of sand. The Greeks were impressed by these watery-looking crystals, and speculated that ice had been compressed by an overlying mountain until it had become permanently solid. When it is purple, presumably because of a trace of iron, quartz is known as "amethyst."

One member of the quartz family exhibits such a striking optical phenomenon that it should be particularly mentioned. Unlike the diamond, which refracts light, this mineral owes its optical properties to interference, which also gives a soap bubble or a film of oil its colors. Presumably, interference may result from fracturing, lamellation or the irregular disposition of water and when this happens to quartz, the result is color at play and the stone is called an "opal."

The manufacture of synthetic gems, such as rubby, sapphire, spinel and emerald, is a relatively recent achievement. By the fusing of powdered aluminum oxide in an oxyacetylene flame and the adding of chromium oxide, a chemically pure and physically faultless ruby can be produced. Synthetic gems have all the good points and few of the faults of their natural counterparts. They are saints without sin; but this makes them less interesting and also less expensive.

"Written With a Pen of Iron, and With the Point of a Diamond"

From earliest times gem stones have figured conspicuously in ceremonials. There was one collection of gems that became the subject of much study and controversy. This was the collection of twelve rare and costly stones that were mounted about 12 centuries B.C. in the breastplate of Aaron the Levite, first high priest of the

Israelites. These stones were about 2 by 2½ inches and on the back of each was engraved the name of one of the tribes of Israel. The color of each stone was appropriate to the tribe and its standard in camp. Moreover, the stones were believed to possess miraculous power. It was held that by changing luster they revealed the guilt of the sinful, portended disease and forecast the outcome of battle.

In the authorized version of the Bible, 1611, the designation of the stones is explicit. For example, "the second row shall be an emerald, a sapphire and a diamond." The sources and size of these stones and the known lack of abrasives that would cut some of the stones in ancient times have aroused the suspicions of lapidarists. Scholars were interested, but not disturbed. They realized that the translators of the Authorized Version had consulted the best works available at the time and had conveyed the thought of the texts beautifully. When King James I in 1604 appointed the most learned in Westminster, Oxford and Cambridge to the number of four and fifty who labored twice seven times seventy-two days and more, or two years and nine months, they produced one uniform translation of the Bible into good English without marginal notes, as King James had instructed them to do. It has been said that no other committee of this size ever accomplished its purpose.

The original texts with which the translators worked were not so explicit as to the naming and arrangement of the stones, and the identification of the stones has been uncertain. For example, the stone that carried the name of Judah was called a "glowing coal." One translation was "ruby." There is no proof that this stone was known to the early Egyptians, and the "glowing coal" actually may have been garnet or red jasper. How would you have translated it? The sapphirus carried the name "Issachar," a son of Jacob and Leah. This stone was described as "like the body of heaven" and having golden spots. The sapphirus probably was the stone we now call "lapis lazuli." The Egyptians valued it highly, demanded it as tribute, and used it in amulets. Lapis has been mined since 4,000 B.C. and the mines are still in operation. The translators rendered the Hebrew word meaning "the smiter" as "diamond." This stone carried the name "Zebulun," who was one of Jacob's twelve sons, for whom a tribe was named. Despite the legend that all twelve stones of Aaron were said to have been engraved, it is obvious that a true diamond could not have been engraved. Ancient seals often were smitten with onyx.

No trace of this remarkable tablet or that of the second temple of Jerusalem has been found. Increasingly tenuous evidence suggests that in 70 A.D. the breastplate of Aaron was taken from Jerusalem to Rome by the Emperor Titus, and in 455 from Rome to Constantinople by the Vandals under Genseric, and then returned to Jerusalem because of fear of disaster. In 615, it has been thought, it was taken from Jerusalem by the Persian king and in 637 from him by Mohammedan Arabs.

"Wisdom Is Better Than Rubies"

By this time it must have occurred to you that the amateur who ventures to collect and polish rocks soon finds himself caught in a web which he cannot resist exploring. And when he does so, he becomes enmeshed in other and still other webs, the centers of which are geology, petrology, optics, crystallography, chemistry, paleontology, the fine arts and history. As a result he never can escape; nor does he wish to. At home he has his rocks and wheels; at odd moments he enjoys the flavor of a stone in his pocket and at night he journeys from the galaxies to crystals as dainty as a timid thought. He learns to work cheerfully, to play diligently, and to live and die without regret.

NEW BOOKLET ON RESEARCH CAREERS

A new booklet, "Decision for Research," has been issued by the American Heart Association as a follow-up to the educational television series of the same name presented by NBC-TV and AHA to stimulate student interest in research careers. The booklet, prepared and published with assistance from E. R. Squibb and Sons, a division of Olin Mathieson Chemical Corporation, gives additional information about planning for a research career. It is obtainable free of charge from local Heart Associations or from the American Heart Association, 44 East 23rd Street, New York 10, N. Y.

Case Presentations

Weber-Christian Disease or Relapsing Nodular Panniculitis

A Report of Four Cases

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Willmar, Minnesota

RELAPSING nodular panniculitis was first described by Pfeiffer in 1892. The third and fourth cases were described between 1920 and 1930 by Weber and by Christian.[1] Since that time the number reported has increased rapidly so that presently over one hundred cases are recorded.[2] The following four cases have clinical and pathologic features which suggest that they should be included in this diagnostic category.

Report of Cases

Case 1.—Mrs. E. F. was a white woman, aged sixty-four, who complained of painful nodules present intermittently for three months on both lower legs. She had fever and malaise for a short time prior to the development of the lesions. Her temperature was 99.8° (0). Physical examination was not remarkable except for the presence of multiple elevated nodules about the left ankle and a single similar nodule over the right Achilles tendon. These nodules were tender, erythematous, and 1-2 cm. in diameter. The lesions about the left ankle appeared in some areas to coalesce. Routine blood studies and urinalysis were normal. The sedimentation rate was 59 mm per hour. A nodule was biopsied. Microscopically the skin itself was described as normal; however, fat necrosis and calcification in the connective tissue were noted. The changes were considered compatible with Weber-Christian disease. The patient was placed on prednisolone 15 mgm. daily. Prompt objective and subjective improvement occurred. The drug was gradually withdrawn over a six-week period. No untoward side effects ascribable to steroid therapy occurred, although the biopsy site healed rather slowly. (Slow healing of biopsy sites has been described repeatedly in conjunction with Weber-Christian disease regardless of steroid therapy.[3]) The patient has been followed eighteen months since therapy was discontinued without a definite recurrence although she maintains she is not entirely well. The area of the biopsy remains slightly indurated, tender, and erythematous.

Case 2.—Mrs. D. D., a white woman, aged thirty-two, complained of painful swellings about both ankles of eighteen days duration. For several days she had been aware of a similar lesion in the region of the right elbow. She further stated that she had felt unwell for one month before the onset of her presenting symptoms and that she had become progressively more "pooped." She had mild chills and fever several nights before her first visit. She had had a mild sore throat intermittently. Physical examination revealed a temperature of 99.2°(0) in the A.M., diffuse pharyngeal injection and a small nodular goiter. Multiple erythematous areas were present about both ankles, coalescing in places. These areas were warm, indurated and tender, but not definitely elevated; however, there was considerable pitting edema about and distal to the lesions. A similar lesion was present on the lateral aspect of the right elbow. Routine blood studies and urinalysis were within normal limits. The sedimentation rate was 17 mm. per hour. A biopsy of a lesion was obtained. Microscopically the skin was described as normal, but deeper sections showed considerable inflammatory infiltrate with some fibrosis. The changes were interpreted as compatible with Weber-Christian disease. The patient was placed on prednisolone 40 mgm. daily with prompt improvement. The steroid dosage was reduced rapidly. A mild exacerbation of the process occurred when the steroid had been reduced to 20 mgm. daily, but subsided when the dosage was held at that level for a time. The patient returned to her home in Indianapolis prior to discontinuance of the drug; however, the steroid was subsequently completely withdrawn without further difficulty. Total duration of steroid therapy was five weeks and no untoward side effects occurred. The patient informs me by letter that she has had no frank recurrence of her difficulty, but further states that she has not been entirely well since the acute episode. Her subsequent symptoms include fatigue, aching and stiffness of various joints. Fourteen months have elapsed since the original episode.

Case 3.—Mrs. L. J., a white woman, aged sixty, complained of tender areas on her legs, aching in the legs and abdomen, fever, chills and sweats, all of one week's duration. Physical examination revealed a temperature of 99°(0) and moderate crepitus of both knees with a slight effusion on the right. A warm elevated erythematous area, slightly over 1 cm. in diameter was present on the left calf laterally. Similar lesions were present below the right patella and over both Achilles tendons. Scattered erythematous areas were noted on both forearms, but these areas were not elevated, indurated, or tender. A complete blood count was normal except for the presence of 79 per cent polymorphonuclear leuko-

Presented before the Minnesota Society of Internal Medicine, Rochester, Minnesota, October 21, 1957.

cytes in the differential white count. The total white blood count was 8,850. Urinalysis was negative. The sedimentation rate was 67 mm. per hour. A biopsy was obtained of the lesion on the left calf and was reported as showing scarring and extensive hyaline change, the overall pattern suggesting scleroderma. Review of the situation with the patient revealed that the active lesion had appeared surrounding an old traumatic scar, which had apparently been biopsied inadvertently. The patient was placed on prednisolone 40 mgm. daily with gradual reduction of the dose. Subjective and objective improvement occurred promptly. An exacerbation of the process occurred when the steroid was reduced to 5 mgm. daily, but subsided again when the dosage was increased slightly. Subsequently the drug was withdrawn without ill effect. Total duration of therapy was seven weeks. No adverse side effects ascribable to the steroid were observed. The patient has been followed eight months after completion of therapy. Six months after the first episode new lesions appeared on the legs which disappeared spontaneously within two weeks. These lesions were not as painful as on the first occasion and there were virtually no associated systemic symptoms. Unfortunately, this episode was not observed by the author. In addition the patient continues to complain of chronic mild aches and pains in various parts of the body.

Case 4.—Mrs. E. V., a white woman, aged fifty-three, complained of swelling and tender areas about the ankles of ten days' duration. She had no other symptoms except dull headaches and discomfort in the right popliteal region of one day's duration. Physical examination revealed a temperature of 98.4°(0), and nonelevated, warm, tender, erythematous areas about both ankles. The lesions were 1-2 cm. in diameter. Other than prominent Heberdeen's nodes, no joint abnormalities were noted. In particular, the popliteal areas were negative upon examination. Routine blood studies and urinalysis were within normal limits. A lesion was biopsied and reported as showing a chronic inflammatory reaction in adipose tissue with some nonspecific granulomas. The skin was not described as abnormal. The pattern was considered consistent with a diagnosis of Weber-Christian disease (Figs. 1, 2). While awaiting the biopsy report, the process subsided to a considerable degree spontaneously. During this period of time a new lesion appeared on the left leg laterally which had an elevated "cord" centrally suggesting a superficial phlebitis. Because of the spontaneous remission, steroid therapy was deemed inadvisable. Three weeks later the process exacerbated with new lesions (similar to the earlier lesions), on the legs chiefly about the ankles. At this time the original lesions could be distinguished because of minimal residual pigmentation. With this exacerbation of the subcutaneous process, the patient noted malaise, headache, and pain in the region of the left shoulder. She remained afebrile. She was placed on prednisolone 40 mgm. daily with prompt remission of symptoms and virtual disappearance of the subcutaneous lesions. The steroid was gradually withdrawn. The total period of therapy was five weeks. This patient developed the only significant side effects in this series from the steroid medication. She became hyperirritable and had considerable insomnia. These symptoms were fairly well controlled with mild sedation. The patient has been followed nine months, states she feels entirely well and has had no evidences of further recurrences.

Discussion

A review of the literature devoted to Weber-Christian disease, particularly recent case reports, cannot fail to leave the impression that the clinical picture associated with the diagnosis of Weber-Christian disease is extremely variable. This fact has been commented on by others.[1,4] Although fever is included in the classic description of the disease, it is apparently frequently absent.[4,5] In this series objective temperature elevation was noted in Case 1 only, although two others described febrile symptoms. Characteristically, the disease is relapsing, but cases are reported where only a single episode is described.[6] In this series, under observation a relatively short time, Cases 1 and 4 had a distinctly relapsing character, although the relapses occurred quite close together. Case 3 may have had a minor relapse.

The greatest variability of all occurs in the response to various forms of therapy. In this series unequivocal response to a steroid, prednisolone, occurred in all cases. The case reported by Crosbie had a similar dramatic response; however, in other reported cases where steroid or corticotrophin therapy was employed, either no response or an incomplete response occurred.[5,7,8,9] It should be noted that in several instances the duration of therapy was very brief and in several the dosage was not mentioned or was quite small. Sandifer reports a case where partial control was achieved with cortisone, but a much more satisfactory therapeutic result was obtained with x-ray therapy.[9] The use of x-ray therapy was not considered in the series of cases being reported.

The rather great variability in the clinical manifestations of the cases described as Weber-Christian disease and the fact that pathologically the appearance produced by inflammation in the subcutaneous fat is similar regardless of etiology inclines the author to believe with Brudno[10] that Weber-Christian disease is not a disease entity, but rather a nonspecific response to a variety of stimuli, in most instances unrecognized.

The problem of differential diagnosis deserves attention. Clinically the cases in this series had

features quite reminiscent of erythema nodosum. This diagnosis can be dismissed, however, because the biopsies reveal a panniculitis. Erythema nodosum is a disease of the dermis, not of the panniculus.

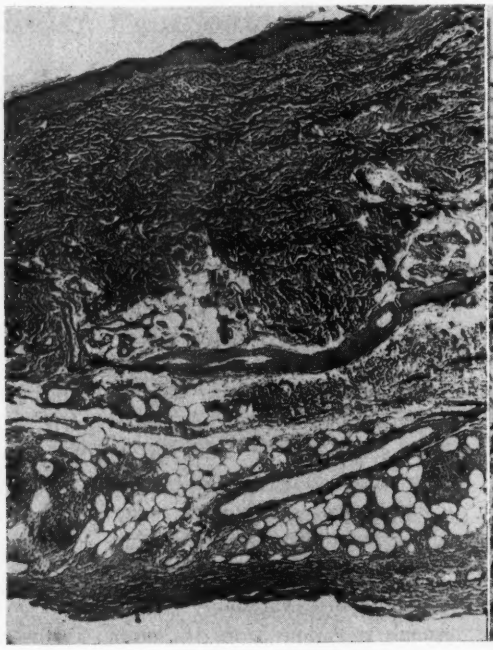

Fig. 1. Low power view from section of skin and subcutaneous tissue, case 4.

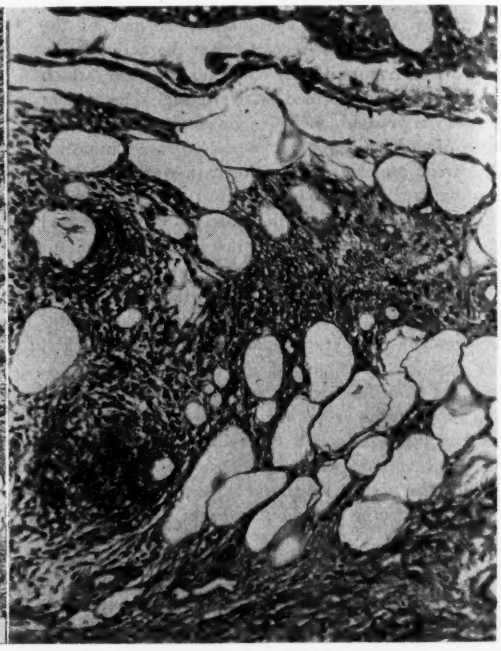

Fig. 2. High power view of the same section of subcutaneous tissue showing a chronic inflammatory reaction in adipose tissue with some nonspecific granulomas.

Michelson describes, in his very fine review of diseases of the subcutaneous fat, certain other forms of panniculitis that are pathologically indistinguishable from Weber-Christian panniculitis. The one group, other than Weber-Christian disease, that the cases in this series most resemble, is one Michelson describes as occurring secondary to stasis disease. Arguing strongly against this possibility here are: (1) the presence of systemic symptoms, (2) the upper extremity lesion in Case 2, and (3) the absence of the skin changes of stasis disease in the biopsy material.

Conclusion

Four cases are presented which can be included within a somewhat heterogenous group called Weber-Christian disease.

It would seem unlikely that this is a single disease entity and until the variants are distinguished might better be called Weber-Christian syndrome or relapsing nodular panniculitis of unknown etiology.

On the basis of the experience in this series, it would appear that short term steroid therapy is well worth a trial for the symptomatic control of an uncomfortable and unpleasant illness.

Addendum

Since the preparation of this paper, two additional cases of Weber-Christian syndrome have been observed by the author. One of these patients was much more toxic than the cases reported and had been hospitalized as a diagnostic problem for over a week when first seen. Both responded to treatment with prednisolone.

Acknowledgment

Robert Hebbel, M.D., Department of Pathology, University of Minnesota, interpreted the biopsies, Cases 1, 3, and 4. Wayne Chadbourne, M.D., then of the St. Cloud Hospital, interpreted the biopsy, Case 2. The illustrations were obtained with the assistance of Dr. Hebbel. John S. Schechter, M.D. The Indianapolis Clinic, Indianapolis, Indiana, provided a follow-up report, Case 2.

(References are on Page A-42)

Benign Calcifying Epithelioma of Malherbe

Report of Case in which Multiple Lesions were Presented

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The occurrence of multiple lesions in benign calcifying epithelioma of Malherbe probably is commoner than was formerly thought. The authors treated a nine-year-old girl who had five such tumors. Simple surgical excision is adequate treatment for this benign lesion.

A LESION encountered somewhat infrequently clinically and pathologically is the calcifying epithelioma of Malherbe. Recently we saw a patient who presented five such tumors.

Report of Case

A nine-year-old white girl was brought by her parents to the Mayo Clinic in February, 1958, for excision of three lesions of the skin. In June, 1956, a firm, nontender tumor had been noted on the left upper arm, and in April, 1957, a similar tumor had been noted on the left leg. Each of these had been excised elsewhere shortly after they had been noted. The three lesions for which our aid was sought were first noted in June, 1957. The maternal grandmother was said to have had sebaceous cysts on the scalp, but there was no familial history of intestinal polyposis and the patient complained of nothing which would involve the gastrointestinal tract.

We found three discrete tumors, one under each mandibular angle and one over the left shoulder (Fig. 1). They were 1.5 to 2 cm. in diameter, and were not tender to the touch; they were irregular and stony hard, with a finely lobulated surface. In each instance the overlying skin was faintly bluish-red and was attached to the tumor, while the tumor itself was freely movable on the underlying tissues. Because of the hardness of the lesions, the possibility of calcifying epithelioma was suggested clinically. Other differential considerations were calcified cyst (sebaceous or epidermal), calcified lymph nodes and calcinosis cutis. The routine roentgenogram of the thorax, however, revealed no abnormal shadows, such as calcareous accretions would make, in the areas in which the lesions were located.

Tissues from the two previously excised tumors were reviewed.* The three presenting tumors were then excised and examined pathologically. Microscopic examination of all the five lesions disclosed similar features, regarded as characteristic of calcifying epithelioma of Malherbe (Fig. 2). They were well-localized tumors, located in the lower dermis, and composed of variously shaped lobules consisting of two types of cells: basophilic cells and shadow cells. The basophilic cells were arranged in clusters and in a bandlike manner, and could be seen in the process of transforming into shadow cells. Areas of calcification frequently were seen within the masses of shadow cells; these areas of calcification were even more notable when the von Kossa stain was used. No areas of cornification or ossification were seen. The connective-tissue stroma contained numerous foreign-body giant cells.

Comment

The original description of this entity by Malherbe and Chenantais[1] in 1880 was followed by numerous reports. Most of these, however, have appeared in the French, German and Spanish literature. The largest series in the English literature are those of Ch'in,[2] who in 1933 collected 116 cases from the world literature and added ten cases of his own, and of Castigliano and Rominger,[3] who in 1954 collected 117 cases which, added to Ch'in's series, gave a total of 243 cases from 1880 to 1950. More recently, Martins[4] has reported an additional 205 cases of his own.

Most authors observe that the lesion is found predominantly in childhood and early adult life, and that it is usually located about the head or neck or arms. Although the tumor usually is solitary, patients with multiple lesions have been reported, and recent studies[4-6] indicate that multiplicity of lesions may not be as uncommon as was formerly thought. In few of these instances

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*This material was kindly provided for our study by Drs. Ralph T. Robinson and Donald W. Penner of Winnipeg, Manitoba, Canada.

of multiple tumors, however, have all the lesions been verified histologically. Sometimes the lesion is mistaken both clinically and histologically for sebaceous cyst.

Fig. 1. Clinical aspect of the calcifying epitheliomas of Malherbe in the case reported. Two of the tumors can be seen: one inferior to the left mandible and one on the superior plane of the left shoulder.

The histogenesis of calcifying epithelioma is not definitely established. Although many theories as to origin have been advanced, several of the more recent authors favor that which assigns the origin to the hair-matrix cells.[7-12] Most authors regard the lesion as benign. Simple surgical excision is the usual recommendation.

Whether benign calcifying epithelioma is a distinct and separate entity has been questioned. King[13] wrote that such lesions actually are mummified epidermal cysts. Lever and Griesemer[11] thought this lesion can be distinguished histologically from epidermal and sebaceous cysts which have calcified and ruptured, with the development of a foreign-body giant-cell reaction. They found basophilic cells and shadow cells in calcifying epitheliomas, while such cells are not present in cysts. On occasion this lesion must also be distinguished from basal-cell epithelioma and squamous-cell epithelioma, especially when either of the foregoing arises in a pre-existing cyst. Here again, the distinction rests largely upon the characteristic basophilic cells seen transforming into shadow cells.

Summary

An attempt has been made to focus attention on the calcifying epithelioma of Malherbe by reporting upon a patient who had five such lesions.

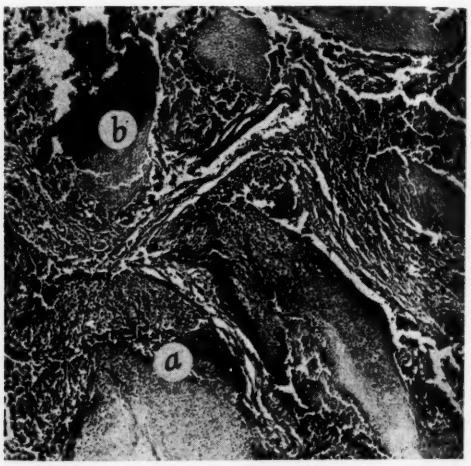

Fig. 2. Characteristic histopathologic features of the calcifying epithelioma of Malherbe which were seen in each of the five lesions in the case reported. *(a)* Lobular masses of basophilic cells are seen transforming into shadow cells. These masses lie in a connective-tissue stroma, in which a foreign-body giant-cell reaction has occurred. *(b)* An area of calcification is seen lying within a mass of shadow cells (hematoxylin and eosin; x50).

We regard this lesion as benign, and we submit that simple surgical excision constitutes adequate treatment.

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(Continued on Page 663)

Editorials

JOHN F. BRIGGS, M.D.
ARTHUR H. WELLS, M.D.
HENRY G. MOEHRING, M.D.

THE PRIVATE PHYSICIAN AND THE HOME CARE OF TUBERCULOSIS

For many years, the greater share of responsibility for the care of patients with tuberculosis has been delegated to specialists in tuberculosis and to local or federal government institutions. Private practitioners as a rule have been pleased to shed this duty. Now, however, due to recent changes in the care of tuberculosis, that responsibility is rapidly shifting back to the home physician. Whether this change will be good or bad will depend on how the personal physician meets this obligation. Those who firmly believe in the private practice of medicine are confident that this trend toward home care will provide not only as good care as in the past but perhaps even better. Others are somewhat skeptical. The fact remains that the care of patients with tuberculosis by their own physicians will challenge both the physicians' ability and the present system of medical practice.

The current problem of home care for tuberculous persons is due largely to remarkable advances in treatment and to effective public health work. Rest in bed is no longer so rigidly enforced, making the care of the patient much easier. Eradication of tubercle bacilli from the sputum often occurs early in the course of treatment, lessening the danger of infecting others. Patients are dismissed earlier from the sanatorium to follow medical treatment at home. With shorter periods in the sanatorium, the number of hospitalized patients has declined, and many sanatoria have closed because of lessened occupancy. With fewer sanatoria, many dismissed patients now find themselves far removed from their hospital and its outpatient care. Because of decreasing case loads, not many physicians are entering the field of tuberculosis. All these factors put a heavier load on the private practitioner.

The problem of caring for tuberculous patients at home is not new, but perhaps we have neglected to face it squarely in the past. There have been many of these patients at home always. Some of these were waiting their turn to enter the sanatorium, others had been dismissed regularly or irregularly from the hospital, while still others preferred to remain under the care of their personal physician. The United States Public Health Service estimates that now about half of the patients with significant tuberculosis are at home, a majority being in the advanced and presumably communicable state. Whether we like it or not, the problem of home care is here to stay and is increasing in importance; it will not go away simply because we refuse to look at it.

Three major aspects of treatment must be meticulously co-ordinated if the home care of tuberculosis is to be successful. The first is the important matter of public health. It is the legal obligation of the physician to report all cases of tuberculosis. From then on until long after all treatment is discontinued, health authorities must supervise the patient regularly in order to encourage him to return to his physician if he does not follow treatment, to notify other health departments if he moves to a new locality, to see that all contacts are properly examined, and to keep the patient from infecting others. At times the health officials must take legal action to control a dangerous patient, a procedure that no private physician wishes to undertake himself. We should all welcome the supplemental assistance of the health officers and give them full cooperation, but it must not be forgotten that the physician in charge is still responsible for the patient's isolation if the disease is communicable.

The second major aspect of home care is the program of treatment. This should be prescribed by those who are experienced in the medical and surgical treatment of tuberculosis, and it is initiated preferably in a hospital or sanatorium. Home care is not being substituted for hospital care. Recent studies indicate that 80 to 89 per cent of patients have at least some period of hospitalization during their disease. Initial hospitalization is so desirable for most patients as to be almost imperative, the length of confinement depending on individual circumstances.

The third aspect, which furnishes the reason for this editorial, begins when the patient is ready for home care under his personal physician. For the home physician to handle his patient intelligently, he must be given complete information

on the previous phases of the illness and projected plans for future care. From then on, the personal physician must be in complete command of the patient. He should not try to lessen his responsibility by assuming that he acts only as the agent of the sanatorium physician, even though he may seek the latter's advice frequently. In order to be proficient in his duty, the physician must, of course, learn much about the modern management of tuberculosis. It is his obligation to see the patient regularly, to encourage him to continue therapy, to watch for complications, to obtain bacteriologic, roentgenologic and other examinations as may be indicated, and to secure consultation with specialists in tuberculosis from time to time. In most well-organized sanatoria, decisions regarding treatment are not made by one physician alone but by several members of the staff in consultation. It is even more important that this plan continue when the patient returns to the care of his own physician, who should seek consultation before making any changes in the program. The hazards of interrupting or discontinuing therapy, of omitting one or another drug of a multiple-drug regimen, or of failing to recommend surgical treatment when it is indicated can be fully appreciated only by those who have seen the tragic results that may follow such action. The conscientious physician welcomes consultation and, in this day, knows that his prestige with a perplexed patient improves as a result. And the wise consultant knows that the attending physician's opinion never must be taken lightly. The two of them must be charitable in their attitude toward each other, particularly regarding treatment. After all, much disagreement still exists even among specialists.

The generally successful results of medical and surgical treatment may have led us into a false sense of security. Modern therapy can be successful only if we remember that the disease itself remains as treacherous and patients as capricious as ever.

The home physician now is being given a chance to show whether private medical practice can handle a difficult and dangerous disease with ability and safety. Although the task will not be easy, he must, and many think he will, do an even better job than that which has been done so well in the past.

CORRIN H. HODGSON, M.D.

USE OF TRUSTS

Most professional and business people have some notion of the nature of trusts, but few have a comprehensive knowledge of the numerous objectives which may be accomplished by their use.

Generally, a "trust" is the holding of property by a "trustee," subject to a duty to apply the property or its proceeds according to the directions of the "donor" or "grantor"—the person from whom it is derived. Any number of beneficiaries may be designated. One or more trustees are named, chosen for particular aptitude to discharge the duties imposed by the trust.

Trusts in their most common form are either inter vivos (created during the life of the donor) or testamentary (created upon the death of the donor, customarily by his will).

Many successful professional and business people find themselves with an accumulation of property which is to some extent greater than necessary to insure their own security. Frequently, the same persons have a very definite legal or moral responsibility to provide for the care, maintenance and welfare of a child or other person who, for one reason or another, is partially or totally dependent upon him.

An outright gift to the needy person may not be the answer because of lack of ability to manage or retain capital. So the benefactor carries on year after year supporting the object of his bounty out of funds produced by the arduous efforts of this successful man, or by careful and time consuming management of his property. Such support must be afforded from funds left after payment of state and federal income taxes at the nearly confiscatory rates applicable to the successful. Here is a typical situation where the inter vivos trust may be the happy solution.

The benefactor may set aside a sum of money or items of property which he does not need for his own support or security. This is done by declaration or deed of trust, naming a carefully chosen trustee. The benefactor (donor) may devote the trust property itself, the income from it, or both to the requirements of the beneficiary. The trustee proceeds to manage the property making distribution to the extent directed and exercising only such discretion in investment and distribution as the trust document allows. The trustee may be instructed in greater or lesser detail just how and when payments from income from the trust property or from income and prin-

cipal are to be made, either to or on behalf of the beneficiary. If the donor has not made previous gifts, then up to $30,000.00 of the amount committed to the trust will be free of gift tax. If the gift is for the benefit of a wife, up to one-half may be free of federal gift tax (and the other half subject to the same $30,000 exemption) if the trust is properly created.

It is to be remembered that to qualify for the greatest tax advantage the donor must divest himself of every vestige of control, benefit or personal interest in the trust property or its income. He may not retain even a possibility of a reversion to him at some later date, but must provide for ultimate distribution either to the primary or to other beneficiaries.

Assuming that the donor has properly divested himself of every personal interest in the trust principal and income, the donor is no longer taxed on the income produced by the trust property at the highest rate applicable in his income bracket but the trustee or beneficiary, depending on the provisions for distribution of income, is taxable at the lower rates applicable to the lower income.

Upon the death of the donor, the trust property is not subject to estate and inheritance taxes unless the trust was made in contemplation of death, that is, for the primary purpose of avoiding taxes incident upon death.

The testamentary trust is a device by which one who is skeptical of the ability of those near and dear to him to manage capital or who fears diversion of such capital by a surviving spouse from the family may insure against these contingencies. At the same time, by carefully considered instructions to the trustee, the man setting up such a trust in his will may provide as liberally as the amount of his assets will permit. At the same time he may, as in the case of an inter vivos trust, prohibit by the terms of the trust any spendthrift commitments which the beneficiary may try to charge against the property.

Such use of trusts as those here described, when carefully worked out to achieve the needs prevailing in each individual case, can and does go far toward producing contentment in the mind of the donor who has wisely provided for those dependent upon him, and also in the mind of the dependent beneficiary whose future is assured and secured by such farsighted planning.

In both types of trust care must be exercised when the beneficiary is a wife or husband to avoid any possibility of sacrificing the possible tax benefits of the marital deduction established by the federal Internal Revenue Code. However, this is the topic of another editorial to follow soon.

RONALD S. HAZEL

THE ROLE OF A DOCTOR'S WIFE

Public Relations

Doctors' wives do not swear by the Oath of Hippocrates, but they learn early in their married lives to know little or nothing about the practice of medicine or their husband's patients, and if they inadvertently find out, not to divulge anything outside the medical family.

We usually use the term Public Relations in signifying the relationship between the medical and non-medical public, but may I make a plea for the relationship between members of the medical profession. Jealousies and misunderstandings develop between doctors for they are human, too, with all the faults and frailties of human nature. These can usually be resolved between themselves if the wives will stay out of the arena. I feel very strongly that this area is out of bounds for doctors' wives. If they get into the act, the whole difficulty is so magnified that it soon becomes a community problem, and both the doctor and the medical profession suffer in community public relations, no matter who is right.

Perhaps I am a little smug in my evaluation of people, but I am annoyed when I am introduced to some doctor's wife and she says, "I am the surgeon's wife." Understandibly, the surgeon is proud of his status but he could not do his work without the team of internists, laboratory personnel, anesthetists, nurses, researchers, and all the others who are part of the medical team which has made his work safer and easier. So the wife who brags in this manner, to my mind, is speaking out of turn. She did not produce her husband, his capable hands and trained mind, or secure the medical team that made his work possible. She should rather be grateful that she is a little part of his world and try to make his supreme efforts in the operating room free from worry about her.

It seems that everything we do has a bearing on Public Relations. Doctors' wives are special people; they are always accepted socially (unless they prove themselves otherwise by word or deed), and it is a great responsibility that we do not

always recognize or care to take. Some wives are of great assistance to their husbands on this score, while others fail and their husbands' work has to get along on its own merit. A case came to my attention where a clinic needed a replacement in medical personnel due to the death of one of the members. One of the older physicians in a neighboring town offered this sage advice: "The doctor who applies will be qualified; it is most important to interview the wife to see if she has the right perspective to live in a smaller town and will be content to let her husband practice his profession as he sees fit."

Just as Big Business is now evaluating both the prospective junior executive and his wife when a promotion is imminent, so it might be a good idea to use the same yardsticks on doctors' wives. I often wonder how many of us could have passed the test, for I know that I have learned a lot in the art of trying to be a good doctor's wife. Each day brings a new challenge. I would like to mention in this field that last Spring the Auxiliary to the Hennepin County Medical Society helped organize the wives of the medical students at the University of Minnesota into an auxiliary to the student AMA. These young women are eager to learn how to be good doctors' wives, and they are going into their life's work with enthusiasm tempered with level heads and a realistic approach. This speaks well for good Public Relations.

Doctors' wives should be interested in all that affects their husbands. They are in a peculiar liaison position between the public and the medical profession, and can do much to effect a happy relationship in their home communities.

We should be interested in all phases of Public Health. This includes the various health fields, from the various clinics to mental health and all its implications from problems of children to those of the aging. We should be informed on the rehabilitation opportunities in our towns. These are the concrete programs which can be exploited through programs put on in clubs, Ladies Aids, PTA's and the like. In fact, this whole program can become so involved that we have time for little else.

What about Hospital Auxiliaries? Here is a wonderful place to spark the lay woman. The doctor's wife should be interested in her Hospital Auxiliary, but she should stress the fact that as the hospital makes her husband's work easier, it also gives the community better medical care, so they both gain. I believe that the best efforts are achieved when the work is cooperative, for in this way the lay person knows that you are interested in his welfare. This is just one field of joint endeavor. No one doctor's wife can do all the community work asked of her, but she should attempt to evaluate the human equation of understanding the people in her community.

We know that our doctors are well trained and competent, but some do not always sell themselves to the public because they cannot or do not take the time to understand a patient's reaction. Here is where the wife in her social contacts, without ostentation, can be charitable and generous in her human concern and thus reflect her husband's concern.

I know of no other profession where a husband and wife are accepted to such a degree as a team, in the promotion of good will in the community, for in such team work the husband does the work and the wife interprets his health work by means of tact, service and understanding.

Being a doctor's wife has many privileges and compensations, but it also has its limitations, mostly in time and energy. It is difficult to make generalizations and evaluations, but all of us believe we are having a rare privilege trying to be a good one.

(Mrs. C. L.) Helen Oppegaard
Immediate Past President,
Woman's Auxiliary, MSMA

DOCTORS, HEART ASSOCIATIONS, AND UNITED FUNDS

As the American Heart Association approaches its second decade as a national voluntary health agency, we find its promise of continued success being threatened by a movement that is serious in nature and large in scope.

Just when we begin to glimpse where and how the answers to strokes, coronary disease and hypertension may be found, we are turned aside from our main task by the necessity of defending ourselves against an organized effort designed to regiment us into a single plan of fund raising. Knowing that doctors, of all people, demand for themselves and champion for others the right of fair and equal opportunity and the privilege of individual enterprise, I am addressing myself to you, the members of my own profession, in the

hope that you will help us to maintain the Heart Association as a free American institution.

I am referring, of course, to the effort now being made by United Funds to force the national voluntary health agencies into giving up their independent campaigns. However, at the outset I wish to make one point crystal clear: we in the heart associations are *not* fighting United Funds; we are striving to continue and expand a scientific program designed to conquer the cardiovascular diseases through the combined voluntary efforts of the medical profession and the public. We regard federated plans of fund raising, especially for local charity causes, as fully worthy of support, provided they are truly voluntary and not forced on either the people or the participating agencies. We certainly want all community chests to succeed, and will do everything in our power, short of participating actively in their campaigns, to help them accomplish their goals.

Now what has this matter of fund raising got to do with the medical profession? As the world becomes more complex and more anxiety ridden, people everywhere, including those here in the United States, are being asked to turn to government for "womb to tomb" security, including socialized medical care.

A major influence restraining this drift toward governmental domination has been the development of a unique and typically American institution, the national voluntary health agency. This is usually an association or society devoted to a limited or specific purpose, such as the prevention and control of a single disease. It often comes into being in response to a profound conviction on the part of individuals—laymen and physicians—that their combined efforts are needed to combat a major health menace. These citizens decide on their own to *do* something—not to rely solely on government. What could be more American than this?

The contributions to medicine made by the national voluntary health agencies during the past decade have been impressive. Polio appears to be on its way out. Cancer's early-detection campaign is saving an estimated 75,000 lives a year. In a half century, the National Tuberculosis Association has spearheaded a 90 per cent reduction in that disease. In just ten years, the Heart Fund has channeled over 25 million dollars into research which has produced vital new methods of diagnosis, prevention and treatment of cardiovascular diseases.

Now here is a very important point: by establishing such national voluntary health agencies, the American people have not only promoted health, they have also protected themselves, and especially the medical profession, from increasing governmental domination of the health field. The Heart Association, the Cancer Society, the Polio Foundation, and others, have acted as *buffers* between private medicine and governmental medicine.

I do not mean to deny to government an appropriate place in the medical field. However, I do believe that the medical profession owes a substantial debt to the voluntary health agencies for helping to preserve the primary interests of private medicine in matters of health.

By providing independent leadership and by giving counsel to governmental health agencies, such as the National Institutes of Health, the voluntary agencies have helped, not only to maintain the integrity of the medical profession, but also to channel the health activities of government into their proper areas and functions. The National Institutes of Health have not suffered; on the contrary they have profited through the existence of the voluntary health agencies. They did and still do look to these agencies to pioneer, to experiment, and to show the way in exploring the health needs of the nation.

The voluntary health agencies also serve as a powerful channel through which the value of the work and achievements of the medical profession and research investigators is made known to the public. Every agency, as a matter of policy, says to the public over and over again: "See your own physician; he is your best protection against disease."

Realizing that a doctor cannot ethically remind his patients that they need him, the health agencies can and do. They extol the family doctor as the first and best line of defense against disease and death, and they back him up with research, education and community service.

It is ironical, therefore, that United Funds have focused attention on the local physician and the local medical society as a point of attack in promoting their campaigns. What usually happens in a community is this:

A small body of citizens, usually local business executives, either self-motivated or persuaded by professional representatives of United Funds, become annoyed by "so many drives," and it is decided to reduce the number of these drives. The

national organization, known as the United Community Funds and Councils, then sends out information and workers to instruct the local group. With or without a preliminary "survey," these workers come up with the surprising answer that the public is in revolt against so many drives, and that a United Fund Plan of "One gift for all—one campaign for all" will solve all the local charity and welfare problems.

The local group are glad to believe that this is the answer to their problem, part of which usually includes the fact that the local Community Chest has been faltering, not to say failing. They are particularly glad to believe in the United Fund plan when they are further told how *easy* it will be. "No more door-to-door solicitations by weary volunteers; no more high-powered campaigns by a multitude of drives," they are told; "merely a single payroll check-off in industrial plants and places of work and the job is done for you."

On this basis, the local group enthusiastically set out to establish a United Fund. Shortly, however, they begin to run into difficulties. Cancer, Heart, and Polio, for valid reasons of national policy, decline to participate in the local United Fund campaign. And so a struggle is precipitated.

Those who start out believing that their objective is to obtain funds more easily for many good causes, suddenly find themselves attacking some of those very causes. As one point of attack, they focus on individual physicians or on local medical societies in an effort to induce them to endorse the United Fund. They use many devices, including personal influence and organizational pressure, to accomplish their purpose.

United Fund people often blame the previous failures of the Community Chest on the health agencies. "Here," they say, "is the reason we have been failing: the health agencies have been siphoning off funds from our community." (They conveniently forget that never in a single year have all the national voluntary health agencies combined received a per capita contribution of more than $1 from the American people.) "People just now happen to be interested in *health,*" they say; "it's a popular cause at the moment. We need it in our campaign to obtain enough money. The health agencies must go along with us, or we'll set up our own health causes and collect the money ourselves. After all, heart, cancer, polio, and the rest are just diseases and one cannot trade-mark a disease."

And so they set up a health "cause" solicitation as part of their campaign, leaving the public to believe that the Heart Association, the Cancer Society, or the Polio Foundation will actually receive the funds, despite advance public declarations by the voluntary agencies that they must decline such funds and will continue to conduct their independent campaigns. Ironically, in the process, United Fund promoters do what they profess to abhor; they establish yet another agency!

The pressures brought to bear by the United Fund people upon the voluntary health agencies in this connection have been almost incredible. They have openly proclaimed that rough pressure methods "with teeth in them" will be used against the agencies that do not participate in local United Funds. Their tactics have included economic threats against, and boycotts of, many private individuals, as well as business organizations. Thus they tell the public not only how to give, but where to give, when to give, and often how much to give.

In the face of such tactics, the national voluntary health agencies have been hard pressed to protect themselves. They have not wished to launch a counterattack, believing that two wrongs do not make a right, and besides they do *not* wish to fight United Funds. They have resorted heretofore merely to passive resistance, relying on the American people to recognize in time the value of the independent way and to find a solution other than regimentation.

Whether we like it or not, the medical profession is directly involved in this controversy. Medicine cannot continue to ignore or condone the threats to itself through the increasing attacks by United Funds on the voluntary health agencies. For United Funds are promoting a movement under which uninformed, though conceivably well intentioned, local laymen are entering directly into national medical fields of health and disease and deciding where and when funds should be spent for each purpose, and *how much*. United Fund people may understand local charity needs, but they know nothing about the requirements of the nationally coordinated programs of medical research being conducted by the voluntary health agencies.

During its early years, the Heart Association participated in over 450 United Funds, and sadly learned not only that the amounts collected were inadequate, but also that devotion and zeal were lost even among dedicated Heart Volunteers when

they succumbed to the siren song of "Once for all."

Today the Heart Association has withdrawn from all but 270 of these Funds. Based on the per capita giving in the remaining Funds, the Heart Association in 1957 would have raised less than half the amount it did raise had it participated in a United Fund everywhere. It therefore becomes forcefully apparent that the Heart program would have suffered a serious setback in research, not to mention all other phases of its work, had the Heart Association been forced to abandon its independence under coercion by the United Funds.

Fund raising, except by taxation, is *not* easy; indeed it should not be easy. Competition is the American way. Health needs like other needs must compete for public support. The law of supply and demand cannot be repealed, and the Heart Association is willing to accept this fact. We believe that the people will continue to supply the funds as long, but only as long, as a major health need exists. When the cardiovascular diseases are conquered, the Heart Association's work will be done.

In the meantime, may I remind you, my medical colleagues, that the Heart Association, and the other ethical national voluntary health agencies, are performing vital services for *you*. They are telling your story to the public; they are protecting you from governmental domination on one side, and from local dictatorship on the other. But most important, along with you they are leading the way towards the control of the major chronic diseases.

If United Funds are permitted to continue to undermine these efforts of the voluntary health agencies, research will dwindle and the conquest of disease inevitably will be delayed. The result will be the needless loss of hundreds of thousands of lives.

Every physician should give most thoughtful consideration to the problems created by the United Fund philosophy and tactics. Freedom is indivisible. It is for all, or for none. The medical profession will help to preserve its own freedom in the future if it insists now, through its county, state, and national organizations, that the ethical voluntary health agencies be freed of further coercion by United Funds.

Individual doctors, who wish to interest themselves and their patients directly in the work of the Heart Association, will receive not only an enthusiastic welcome, but also the satisfaction of contributing in an important way to a volunteer group, whose sole purpose is to help all physicians in their fight against disability and death.

ROBERT W. WILKINS, M.D.
President, American Heart Association

THE ROLE OF THE BASIC SCIENCES IN MEDICINE

IV. Recruitment of Basic Medical Scientists

There is an astounding paradox in the very considerable increase in the availability of money for basic scientific research in the United States and the increasing difficulty in recruitment of top flight young brains into basic medical science careers. One would have supposed that the increased flow of money into basic science would have resulted in attracting a correspondingly larger number of bright young people into such careers. Actually, the basic medical sciences have not fared very well in this regard. There are undoubtedly many factors involved in this result. For one thing, the economic rewards from the practice of medicine have increased at least twice as much as have the salaries of medical scientists and therefore the "economic penalty," so to speak, of an academic career has increased sharply in the last ten years. Consequently, fewer medical graduates go back into basic science careers. Another factor may be the greater allure today of physics and chemistry for scientifically minded youngsters. The spectacular achievements in the fields of atomic chemistry and physics in recent years have caught the imagination of many bright young minds. Furthermore, there is a syphoning off from graduate study in any field of science by the immediate allure of jobs for college graduates in chemistry, physics, mathematics and engineering in various branches of industry. The Federal government put over two billion dollars into applied research and development in 1957 as compared with a little over two hundred million into basic research. The applied research money unquestionably drained talent from basic research. When a bachelor's degree graduate can immediately get yearly salaries in industry greater than he could expect in academic work after earning a doctorate, it is not surprising that many would choose the easier course. Especially if real or expected family responsibilities are on his mind, the young man will think a long time

before rejecting immediate economic comfort for greater long-term intellectual satisfaction.

A further factor in the situation is the undoubted deterioration of teaching in the sciences and in mathematics at the secondary school level in the United States. School Boards have not been willing to put the increased support that they have poured into athletics, manual arts, home economics, for example, into their science programs. In fact, they have frequently built up these other programs at the expense of the development of the subjects with intellectual content.

In this era of scientific and technological development in the United States, the community cannot afford to lose the services of the half of the superior brains among high school graduates who do not go to college. Three years ago Dr. Alan Waterman, Director of the U. S. National Science Foundation, asked "Why do more than half of our high school graduates deemed fully qualified for college work fail to go to college? We already know that only part of the problem is economic. One of the problems is that of motivation. What other factors are involved and what can be done to correct them? There is now a critical shortage of teachers of mathematics and science in the high schools. Clearly, greater interest in science and mathematics could be stimulated by improved teaching."

The medical profession in the United States has a stake in this situation and is in a position to do something constructive about the problem. Physicians have the same reasons that every citizen has for wanting to see the community prosper. Each physician who is a parent has the same interest as every other parent in wanting the best of educational opportunities for his children. But the physician has an opportunity, shared only by other scientifically trained persons in the community, to speak with some competence based upon education and experience about the absolute necessity to improve educational opportunities in mathematics and the sciences at the high school level. Without becoming political office-holders, physicians can nevertheless exert great influence in their communities by expressing their informed opinions, especially upon nonpartisan issues such as educational policy and support. Members of Boards of Education themselves are almost invariably "non-experts" and, failing assistance from competent community advisors, must take most of their ideas from school administrators who are themselves subject to great pressures. For example, the pressure of alumni and others to promote athletics at the expense of scholarship is virtually a universal phenomenon. Then there are the pressures from special interest groups among secondary school teachers themselves, such as the home economics and the manual arts groups. Frequently, State Departments of Education are of no great help because the professionals in educational administration have in general had no background whatsoever in science themselves and have an inadequate comprehension of the problem. This, it would appear, is one of the prime reasons for the crisis in scientific manpower which this country faces today.

The physician and other persons with scientific training in every community in the land could perform an important patriotic function by working at the local level to improve science teaching in the secondary schools. Only by such a massive attack on the problem will the general scientific manpower shortage be corrected, and specificially only by encouraging more creative young minds to go into the basic medical sciences will the future of medical progress be secure.

MAURICE B. VISSCHER, M.D.

THE PATIENT WITH ACUTE MYOCARDIAL INFARCTION

II. Management of the Acute Phase

When the diagnosis of acute myocardial infarction has been confirmed with the aid of the electrocardiogram and determinations of serum transaminase, the second phase of management confronts the physician. The diagnosis, when established, does not carry with it an optimistic therapeutic outlook such as is true at this time for many of the infectious diseases and even for some of the neoplastic diseases. As physicians we must accept the fact that acute myocardial infarction is the consequence of an unknown quantity and quality of circulatory impairment to the nutrient supply of the myocardium and, consequently, both immediate and long-term prognosis cannot be confidently predicted for any individual patient. We also must subscribe to the seemingly heretical fact that many individuals will survive and recover full cardiac functional reserve without treatment or even without recognition that myocardial infarction has occurred, whereas others who have re-

ceived optimal care by modern medical standards will die of acute myocardial infarction. In brief, the most important apparent factor determining recovery or death of this type of patient is related to this unpredictable inherent capacity of the individual's heart to continue to function with a life sustaining rhythm and with sufficient strength to support life.

Now that the balloon of our therapeutic excellence has been punctured, let us in part repair the puncture by indicating the value and possible accomplishments of the physician in the management of the patient with acute myocardial infarction. Although the physician's care and treatment may not be specifically curative for the heart attack, it continues to be the important factor in the management and prevention of complications and in that significant phase of the art of healing which is the alleviation of suffering. During acute myocardial infarction the attending physician can and should play a role similar to that of the director of a construction project. With careful and continuous observation of his project, which is the healed patient, he will cause to be utilized at the proper time the measures needed for any exigency which arises. At the appropriate time he will utilize drugs for the relief of pain, oxygen, and sedatives. He will be alert to the appearance of shock or cardiac arrhythmias and be timely in his use of vasopressor drugs and anti-arrhythmic drugs. Evidence of failing cardiac compensation will be attacked at his discretion with restriction of sodium, digitalis preparations, and diuretics. The patient's morale, disturbed by his unaccustomed rest program and sudden illness, will be supported by an optimistic attitude as well as sufficient explanation to prevent worry and apprehension.

There can be no routine or usual program which is honestly applicable for management during hospitalization. Observations at frequent personal examinations and by the nursing personnel, and data supplied from laboratory examinations must all be carefully weighed and used in making decisions concerning the measures which will best support the patient in his acute illness. Such careful individualization reduces the incidence of the more frequent errors of omission and commission. The mildly ill patient will not be overtreated or overly restricted, and the early signs of complicating problems will be recognized and adequately managed before they threaten serious consequence.

The prescription of anticoagulant drugs during myocardial infarction has now come of age with 10 years of application. In addition to the actual prophylactic value of this measure, the management of such therapy is improving the over-all care of the patient since careful regulation of the anticoagulant insures careful observation of the patient and consequent early awareness of any irregularities in his convalescent course. Although the nonspecificity of anticoagulant therapy is well recognized, and this, when taken together with the potential hazard of hemorrhage, has led to understandable doubts as to its necessity by its critics, it still remains the principal addition to the medical management for the heart attack which has appeared in this generation. In the absence of the well-recorded contraindications and with the availability of an adequate laboratory for the frequent determination of prothrombin activity, anticoagulants offer the only reasonable approach at this time directed at prevention of vascular occlusive disease of a thrombo-embolic type. With the limited ability to make specific alterations in the vascular disease resulting in myocardial infarction, the theoretic nonspecific benefits of anticoagulants should not be denied any patient during his hospitalization for acute myocardial infarction when contraindications are absent.

MILTON W. ANDERSON, M.D.

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES

After almost three years of planning, the Educational Council for Foreign Medical Graduates opened its doors on October 1, 1957, at 1710 Orrington Avenue, Evanston, Illinois.

What Functions Will It Serve?

It will distribute to foreign medical graduates around the world authentic information regarding the opportunities, difficulties and pitfalls involved in coming to the U. S. on an exchange visitor or exchange student visa in order to take training as an intern or resident in a U. S. hospital, or coming on an immigrant visa with the hope of becoming licensed to practice.

It will make available to properly qualified foreign medical graduates while still in their own country a means of obtaining ECFMG certification (a) to the effect that their educational credentials have been checked and found meeting minimal standards (eighteen years of formal edu-

cation, including at least four years in a bona fide medical school), (b) that the command of English has been tested and found adequate for assuming an internship in an American hospital, (c) that the general knowledge of medicine as evidenced by passing of the American Medical Qualification Examination is adequate for assuming an internship in an American hospital.

It will provide hospitals, state licensing boards, and specialty boards which the foreign medical graduate designates, the results of the three-way screening available.

What Functions Will It Not Serve?

It will not serve as a placement agency either for interns or residents. Placement arrangements must be made by the foreign medical graduate directly with the hospital of his choice or through the National Intern Matching Program.

It will not attempt to evaluate the teaching program or inspect any foreign medical school. Its program is based not upon evaluating the school from which the candidate graduated but upon evaluating the professional competence of the individual.

It will not act as an intercessor for foreign medical graduates having problems under discussion by state boards of medical licensure or specialty boards. If the foreign medical graduate asks that the results of his three-way screening be sent to a designated board this will be done, but the ECFMG has no right and no desire to review the decisions of the properly constituted state licensing boards and American specialty boards.

Who Is Sponsoring the ECFMG?

Sponsors of the new agency are the American Hospital Association, the American Medical Association, the Association of American Medical Colleges and the Federation of State Medical Boards of the United States. Providing funds to support it through the first two years of its existence are the sponsoring agencies and the Kellogg Foundation, and the Rockefeller Foundation.

The ECFMG has been legally incorporated in the State of Illinois and is operating in the first year of its provisional approval as a tax exempt organization under Section 501 (c)(3) of the *Internal Revenue Code of 1954*. The ten-member Board of Trustees includes two representatives from each of the four sponsoring agencies and two representing the public at large (one named by the Department of Defense, the other by the Department of Health, Education and Welfare). The President of the Board of Trustees is Dr. J. Murray Kinsman, Dean of the University of Louisville School of Medicine. The Executive Director is Dr. Dean F. Smiley, former Secretary of the Association of American Medical Colleges.

What Are the Mechanics of the Examination?

The ECFMG's Examination Committee will select the items for two examinations a year from the National Board of Medical Examiners' pool of questions. The National Board of Medical Examiners will use as many of its fifty presently constituted U. S. examination centers as will be required and will establish examination centers abroad in numbers as found required to meet the need.

The National Board of Medical Examiners will proctor the examination, score and analyze the results, and turn them over to the ECFMG's Examination Committee for final evaluation and action.

What is the Charge to Be?

Foreign medical graduates already in this country will be billed for $50.00 covering the cost of the three-way screening. This will include $15.00 for the evaluation of credentials and $35.00 for the American Medical Qualification Examination.

Foreign medical graduates abroad will be billed the $50.00 only when they pass the screening, and receive a position in an American hospital or are otherwise earning American dollars.

American hospitals receiving screened candidates will be billed $75.00 for each such candidate accepted.

What Are the Target Dates for Various Services?

The answering of correspondence began October 5 and has been kept current since that time. The translation, interpretation and evaluation of credentials have already begun.

The first American Medical Qualification Examination for foreign medical graduates already in this country was held March 25, 1958. The second will be held September 23, 1958. The target dates for the 1959 examinations for foreign medical graduates both here and abroad are set for February 17 and September 22.

PHYSICIAN-HOSPITAL RELATIONSHIP
A Resolution

WHEREAS, a wise and foresighted legislature of the State of Minnesota has written laws in Minnesota prohibiting the practice of medicine by corporations and individuals not licensed physicians, and

WHEREAS, the American Medical Association has repeatedly studied the problem and has stated in 1943 that the "House of Delegates of the American Medical Association is opposed to the division of any branch of medical practice into so-called technical and profession factions," and later in 1951, that "the practice of anesthesiology, pathology, physical medicine and radiology are an integral part of the practice of medicine in the same category as the practice of surgery, internal medicine or any other designated field of medicine," and in 1955 reaffirmed its position on these matters.

THEREFORE BE IT RESOLVED, that the Minnesota State Medical Association first, officially recognizes the specialty of Anatomical and Clinical Pathology as the practice of medicine; second, reaffirms the philosophy that in-hospital and outpatient diagnostic laboratory services are in fact the practice of medicine and thirdly, in future contracts or actions relating to laboratory medicine actively reaffirms the belief in the legal control of all medical laboratory facilities in the State of Minnesota by licensed doctors of medicine.

Passed by: Committee on Hospital and Physician Relationships, Committee on Resolutions, House of Delegates, Minnesota State Medical Association, May 23, 1958.

ARTERIOGRAPHY AND CARDIOANGIOGRAPHY

(Continued from Page 643)

Case 3.—A twenty-eight-year-old woman who had known congenital heart disease since childhood. Five years prior to her recent hospitalization, cardiac catheterization suggested an interventricular septal defect with pulmonic stenosis. Surgery was undertaken at that time to correct the pulmonic stenosis. The surgical impression was that of an aortic-pulmonic window.

Recent catheterization studies still suggested an interventricular septal defect with pulmonic stenosis. Selective angiography was done (Fig. 3.) to evaluate the ascending aorta. No aortic-pulmonic window or patent ductus was found, which confirmed the catheterization findings. Incidental delineation of the coronary vessels shows another use of this procedure for study of many portions of the vascular bed. Several illustrations of coronary artery studies in dogs will not be included in this paper.

Case 4.—A sixty-eight-year-old man who developed a pulsating mass in the right hemipelvis. Percutaneous aortography was considered too dangerous.

Selective angiography (Fig. 4.) was performed by inserting a catheter to a point below the renal arteries. This study confirmed the presence of a fusiform aneurysm of the right external iliac artery, which was subsequently removed at surgery.

Case 5.—A sixty-year-old man, known to have a carcinoid syndrome, developed gradually increasing ascites and dependent edema. In order to exclude a physical obstruction of the inferior vena cava, which might be amenable to surgery, a catheter was introduced into the inferior vena cava. The latter, including the portal system and right heart (Figs. 5a and 5b), were completely delineated, and no organic obstruction was present.

Summary

The above cases illustrate only a few applications of angiography in the preoperative work-up of diagnostic problems.

737 E. 22d Street
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EPITHELIUM OF MALHERBE

(Continued from Page 652)

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President's Letter

COMMUNICATION IN MEDICINE

One-hundred and some years ago, the American Medical Association was formed and medicine became a relatively homogeneous group. About fifty years ago, segmentation began to appear and physicians began to group themselves according to specialties less broad than the profession of medicine. As this process continued, the ways of the various specialties diverged further and further, until about ten years ago certain members of the profession had trouble getting their patients into hospitals or caring for them after they were there. Understanding among the groups had diminished to a low point. Communication between the segments almost ceased. The last specialty group organized about that time, and things have improved since then. Throughout this period, various segments of the profession at times have taken it upon themselves to speak for the profession as a whole—indeed this still happens occasionally—sometimes to the embarrassment of the others.

Before World War II, lay health organizations began to be formed, usually devoted to a single disease. This movement has spread until there is hardly a disease left without a lay society to study, to popularize and to try to prevent it. Most are sincere, hard working and helpful. A rare society seems to exist for the profit of its promoters. But regardless of their value—and most are valuable—they also tend to speak for medicine, or at least that part of medicine in the general area of the disease in which they are interested. Unfortunately the fields tend to overlap, or the problem becomes less acute and the organization has to expand its field to continue to exist. Competition follows, for areas of activity and for public finances and for professional talent and advice.

"Third parties" have entered into the economic phases of medicine.

In all these areas—the professional specialty groups as opposed to the general profession, and the specialized lay organization, scientific and economic, as opposed to the profession of medicine in all its branches—communication between the groups would decrease the inevitable friction, the unnecessary duplication, and the unrewarding competition. If any part of the profession can serve as a clearing house, as a center of communications, surely it must be the organization of all the physicians of the state, the State Medical Association. This is not to say that the State Medical Association should make any attempt to control all the ideas, but it is to say that there should be far more effective communication between the elements of the profession and between the outside agencies affecting the profession and the profession itself. And it is to say that the logical and the reasonable center for this communication is the State Medical Association as represented by its House of Delegates and more specifically by its Council.

Horatio R. Sweetser

President, Minnesota State Medical Association

Medical Economics

Edited by the
Committee on Medical Economics,
Minnesota State Medical Association
George Earl, M.D., Chairman

NEW TRIAL ON SALE OF DRUGS ORDERED BY COURT

A new trial has been ordered by the Minnesota Supreme Court in a case which the Hennepin County District Court had previously ruled that supermarkets and grocery stores could sell certain drug items.

Dissenting from the decision was Chief Justice Roger Dell.

Products involved in the case are: Bufferin, Aspirin, Anacin, Bromo-Seltzer, Alka Seltzer, Pepto-Bismol, Pinex, Murine, Ex-Lax, Feen-a-mint, Sal Hepatica, Bromo-Quinine, Asper-Gum, Lysol, 4-Way Cold Tablets, Castoria and Vick's Va-Tro-Nol.

The Court majority, in ordering a new trial, held that the state should have been permitted to present whatever evidence it had to show, whatever danger, if any, the uncontrolled and unsupervised sale of the items presented to the public health.

Justice Dell said the majority opinion "admits that the state failed to present a single instance in which the use of any item enumerated in the complaint, purchased in a grocery store or supermarket, injured the safety, health, comfort, or welfare of anyone."

The case was brought by the state against Red Owl Stores, Inc., and Groves-Kelco, Inc., a wholesale distributor. The state sought a ruling to bar sale of the products by stores other than drug stores.

PHARMACY LAWS CRITICIZED

An organization known as the Affiliated Merchants Association of Minnesota, Inc., has been sending circulars and other printed material to grocery stores and other outlets throughout Minnesota.

These circulars criticize the state laws governing the sale of medicine, as well as the regulations of the Board of Pharmacy. The Affiliated Merchants Association holds that the State Board of Pharmacy seeks to prohibit the sale of drugs and medicine in—all—retail outlets other than drug stores and it plans to eliminate emergency health station permits and licenses.

GOVERNMENT CHARGES WONDER DRUG PRICE-FIXING

The United States Government has charged six major drug firms with fixing the prices of wonder drugs at arbitrary, artificial, and non-competitive price levels.

The charges brought forth by the Federal Trade Commission were the result of a two-year study.

A prompt denial by industry spokesmen followed the government action.

The commission contends that the six accused firms have an absolute monopoly in sales of tetracycline drugs which include Aureomycin, Terramycin and Achromycin.

The agency said the tetracyclines are the largest selling antibiotics by dollar volume. Developed within the last ten years, they are called broad spectrum drugs because they attack a wide range of disease-breeding microbes.

The accused companies are: Chas. Pfizer & Company; American Cyanamid Company; Bristol-Myers Company; Olin Mathieson Chemical Corporation, all of New York City; Bristol Laboratories, Inc., Syracuse, New York, and the Upjohn Company, Kalamazoo, Michigan.

The commission action is aimed at cease and desist orders requiring the companies to stop the alleged price fixing. Commission complaints never call for punitive action and are civil rather than criminal in nature.

Cyanamid and Pfizer accounted for more than 47 per cent of all sales of antibiotics in 1956, the most recent year for which statistics were cited in the commission's study.

Cyanamid manufactures drugs through its Lederle Laboratories division. Olin Mathieson pharmaceuticals are made by its E. R. Squibb & Sons division. Bristol-Myers and Bristol Laboratories are under a single management.

Industry statements compiled by the Associated press included these:

W. G. Malcolm, President of Cyanamid: "Cyanamid has not engaged in any price fixing and has not em-

ployed any unfair methods of competition or any unfair or deceptive acts or practice in its pricing or its use of patents and licenses in the conduct of its antibiotic business."

John E. McKeen, President of Chas. Pfizer and Company: "Pfizer has never engaged in a conspiracy, never misused its patents, never fixed prices, and wields no monopolistic powers."

Dr. E. Gifford Upjohn, President of the Upjohn Company: "This complaint has been studied in detail by officials of the Upjohn Company, who are convinced that the charges are completely unfounded. It is the intention of the Upjohn Company to defend its position and prove conclusively that these charges are untrue."

Frederic N. Schwartz, President of Bristol-Myers Company: "I can state without qualification that these charges are baseless and that this action will be defended vigorously with all the resources at our command."

Industry must answer the complaint within thirty days. October 1 has been tentatively set as a hearing date.

The 361 page FTC report noted that repeated price cuts in early antibiotics, including procaine penicillin and Streptomycin, were made prior to 1951. Comparable drops since that date were not forthcoming in spite of significant shifts in their relative market importance.

The report further stated that in 1956 the industry had profits before taxes of thirty-seven cents on each dollar of sales of broad spectrum antibiotics. The figure for the newest penicillin products for which companies have exclusive manufacturing rights was even higher . . . forty-two cents.

On the other hand, production of older penicillins was carried on at a loss from 1952 through 1956. And Streptomycin production ran a deficit from 1953 through 1956.

For all antibiotics, according to the report, pre-tax profits averaged 28.5 per cent of sales in 1956 compared with 18.3 per cent for the chemical industry and 14.6 for all manufacturing industries.

In recent years, pre-tax profits on antibiotics have ranged from 19.3 cents per dollar of sales in 1952 to 34.5 cents in 1951.

The report shows that actual production costs of wonder drugs have dropped since 1950, but that sales and promotion, research and administrative outlays of drug firms have risen.

Production absorbed 39 cents of each sales dollar in 1956 compared with 44.4 cents in 1950. Sales and advertising expenses amounted to 21.6 cents, up from 12.9 cents in 1950. Research outlays increased to 6.7 cents from 4.4 cents and administrative and other costs rose to 8.7 cents from 7.6 cents.

The report also spelled out markups on wonder drugs. Drug companies generally sell their products to wholesalers from 15 to 21 per cent less than the price which wholesalers charge retailers. The margin between the price to retail druggists, hospitals, and physicians and the list price for consumers is ordinarily 40 per cent.

VARIATIONS IN DRUG PRICES

Variations in the prices of various drugs and who is to blame were discussed in a recent article published in *Drug Topics,* the bi-weekly newspaper of the retail druggist trade.

The article pointed out that a prescription with ingredients costing $1.40 varied in cost to the patient all the way from $1.75 in Washington, D. C., to $7.50 in Bloomfield, New Jersey. Another example cited a prescription in which ingredients cost 50 cents, varying in the price paid by the patient from $1.50 in Baltimore, to $3.00 in Billings, Montana.

Prices for a bottle of fifty tranquilizer tablets ranged from 95 cents to $4.95 in New York City.

A recent Public Health Information Foundation survey indicates that 25 per cent of the persons who complained about high drug prices blamed the retail druggist, 10 per cent blamed doctors, and one person in fourteen blamed the manufacturer.

The following answers were received by Alfred C. Roller, writer for the North American Newspaper Alliance, in a poll which he conducted among representatives of the key group.

The New York Citizens Committee for Children reported physicians often practiced the writing of prescriptions calling for brand name drugs at high prices, which would be lower priced if called for by their scientific names.

The medical director of a large New York hospital echoed the belief and said even further economies could be made if doctors would write prescriptions only for the amount of a drug needed instead of for larger quantities often wasted.

Representatives of the drug manufacturing industry declared high prices are necessary to pay for the research which develops the drugs. More than $1.25 million was spent in such pursuits last year, and it must be paid for, they say.

They also point out that although consumer prices have increased ninety-eight per cent since 1935, the cost of prescriptions rose only 37 per cent.

Calvin Berger, President of the American College of Apothecaries, declared that many overcharges are "due to ignorance rather than a deliberate attempt to overcharge."

Calling for a prescription-pricing system, he pointed out that under present practices, it is impossible for a druggist to fill a prescription for less than a dollar and show a profit.

Representatives of the retail druggists pointed out that they must carry large investments in drugs to fill their prescriptions, and that many of the drugs do not turn over fast enough to make a profit unless there is a high charge to cover the investment costs. Many drugs which move slowly become dead stock. Someone has to pay for them, too, the druggist pointed out, and that someone is usually the customer.

HEALTH INSURANCE ABUSES PROVE COSTLY

Needless costs, estimated at $100,000,000 annually, are being suffered by the health insurance industry because of hospitals and physicians who "first check a patient's insurance before setting their fees."

This fact was recently disclosed in an address presented by Allen Dorfman, President of the Union Insurance Company at a National Association of Insurance Commissioners meeting in Chicago.

Dorfman suggested the following solutions:

1. A pooling arrangement in which all health insurance companies band together to protect themselves from high-risks and overcharging, similar to pooling arrangements now in effect by auto insurance companies.

2. The filing of rate schedules by all hospitals and physicians, showing exact fee and cost structures. This would eliminate "selective" charges by physicians who "check and charge" accordingly. It would also protect against what Dorfman described "current hospital practices of padding 'miscellaneous' charges for drugs, medicines, laboratory fees, et cetera."

According to Dorfman, hospitals and doctors equally share responsibility in abuse of health insurance benefits "with needless costs estimated at $100 million a year."

COST OF LIVING RISES 105 PER CENT IN TWENTY YEARS

Living costs have risen an average of 105 per cent in the twenty-year period between 1938 and 1958, including World War II and the Korean War. This fact was disclosed in an Associated Press dispatch, dated July 24, 1958.

The survey noted that on the average, something which cost one dollar in 1938, now costs $2.05.

According to the cost of living index released by the Federal Government during the last week of July, a rise of one-tenth of one per cent was noted from May to June of this year. This marks the twentieth living cost rise record set in the last twenty-two months.

Statistics prepared by Government experts show that from 1938 to 1943 consumer costs rose 23 per cent; from 1943 to 1948, 39 per cent; from 1948 to 1953, 11 per cent; and from 1953 to 1958, under the Eisenhower administration, 8 per cent, a composite of many different changes.

During these two decades, the rise in cost of various family budget items exceeded the 105 per cent living cost average, while others did not advance accordingly.

The cost of gas and electricity rose only 11 per cent. However, during that period, the cost of coal and fuel oil jumped nearly 129 per cent.

Hospital costs rose nearly 300 per cent; doctor fees increased 84 per cent; men's haircuts, 206 per cents; gasoline, 69 per cent; household appliances, 33 per cent; newspapers, 124 per cent; and movie admissions, 120 per cent.

Cost of men's clothes, however, rose 110 per cent; women's, only 78 per cent.

In the 1953-58 period, food has increased 7.8 per cent; housing, 8.6; rents, 11; gas and electricity, 9.7; coal and fuel oil, 6.3; and clothing, 1.8 per cent. Hospital costs rose 33 per cent; hospitalization insurance the same; shoes, 12.7; haircuts, 23.1; movies, 24; and newspapers, 20 per cent.

In the past five years, substantial price declines were also noted. Appliances, probably due to price discounts, declined 15 per cent; including TV sets, 6 per cent; radios, 10 per cent; refrigerators, 33 per cent; vacuum cleaners, 23 per cent.

A pair of women's nylon hose now costs 13 per cent less than five years ago; men's pajamas, 1 per cent less; bedsheets, 8.3 per cent less; and used cars, 12.6 per cent less.

MINNESOTA BLUE SHIELD—BLUE CROSS

Minnesota Blue Shield subscribers used their contracts much more often during the first half of 1958 than they did during the same period in 1957.

During the first six months of 1958, Blue Shield received Medical Service Reports involving 180,604 eligible services of physicians rendered to subscribers, or 31,245 services more than the number which were paid by the Plan during the first half of 1957. For these services Blue Shield paid doctors $4,919,097, an average of over $819,000 each month.

In the same six months of 1957, allowances were provided for 149,359 services to subscribers. Blue Shield payments for these services in 1957 totaled $4,218,673. Both the number of physicians' services and Blue Shield payments for their services during the first half of 1958 exceeded by over 16 per cent the number of services and the amount paid for them during the first six months of 1957.

While the number of Blue Shield participant subscribers increased 26,362 between July 1, 1957 and June 30, 1958 or from 849,556 to 875,918, the number of Plan B subscribers increased 27,989. Plan B participant subscribers numbered 90,391 as of June 30, 1958 as compared with 62,402 such subscribers on the same date last year.

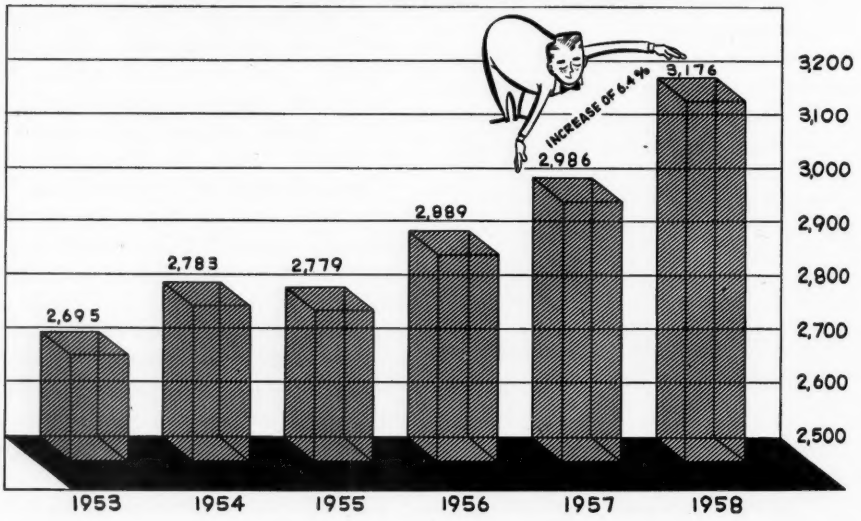
Minnesota Blue Cross payments to hospitals for participant subscribers' care continues at an all time high through the first six months of 1958. Over 108,600 participant subscribers received in excess of $16,800,000 in Blue Cross benefits for 676,386.7 days of hospital care during this first six months period.

This year to date utilization represents 510 cases and 3,176 days paid per year per 1,000 contracts protected, an increase of 6.4 per cent in frequency of subscribers' usage compared to the 488 cases and 2,986 days paid per year per 1,000 contracts protected during the same period of the year 1957.

The accompanying chart shows the five-year trend of frequency of subscribers' usage in terms of the number of days paid per year per 1,000 contracts protected during the first six months of the years 1953-1958.

The increase in frequency of subscribers' usage of Blue Cross benefits is a major factor in the spiraling trend of Blue Cross payments to hospitals.

FREQUENCY OF SUBSCRIBERS' USAGE OF BLUE CROSS BENEFIT DAYS
COMPARISON OF
NUMBER OF DAYS PAID PER YEAR PER 1,000 CONTRACTS PROTECTED
AVERAGE OF FIRST SIX MONTHS' EXPERIENCE



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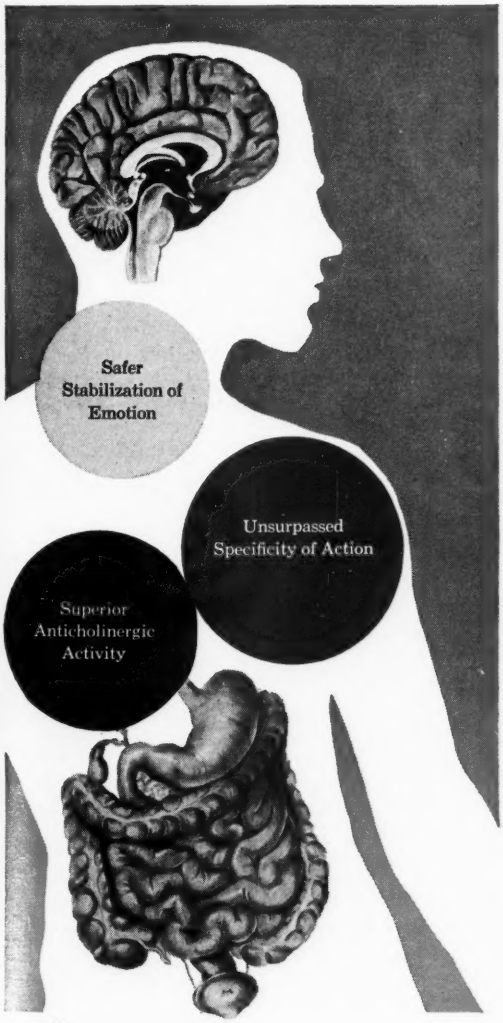

PRO-BANTHINE WITH DARTAL offers you a new, specific and reliable control of visceral motor disorders, especially when these disorders are induced or aggravated by psychic tensions or anxiety.

Pro-Banthine has won wide clinical acceptance as the most effective drug for controlling gastrointestinal hypermotility and hypersecretion.

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The combination of each drug in fully effective doses in Pro-Banthine with Dartal gives a new means of approach to the medical management of functional gastrointestinal disorders mediated by the parasympathetic nervous system.

Specific Clinical Applications: Functional gastrointestinal disturbances, gastritis, pylorospasm, peptic ulcer, spastic colon (irritable bowel), biliary dyskinesia.

Dosage: One tablet three times a day.

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Committee Action

First Aid and Red Cross
Blood and Blood Banks
Maternal Health

Following is a brief statement regarding the various activities in which the Committee on First Aid and Red Cross and the Committee on Blood and Blood Banks participated in 1957.

Committee on First Aid and Red Cross

The problem of ambulance care was referred to the Committee on First Aid and Red Cross, and an exhibit was prepared and shown at the annual state meeting held in Minneapolis May 22, 23 and 24, 1958. Various problems which arise in connection with this project will be studied and dealt with in the future. The council of the State Medical Association has approved of this committee's offering what help it can to improving ambulance care in the state.

Committee on Blood and Blood Banks

The Committee on Blood and Blood Banks has been more or less involved with the civil defense problem of blood transfusion in case of disaster. The first fundamental step has been taken by the approval of the House of Delegates of the Committee's recommendation that all citizens of Minnesota be blood grouped and the Rh factor determined without compulsion. This will permit a solution of what otherwise was an impossible situation of making arrangements for blood transfusions in case of disaster. For one reason or another, this Committee's work is never finished.

JOHN S. LUNDY, M.D., *Chairman*

Committee on Maternal Health

During 1957, the Committee on Maternal Health continued their state-wide study of maternal deaths through their sub-committee, the Minnesota Mortality Study Committee.

The Committee approved a study of the influence of aseptic meningitis (ECHO 9) during pregnancy on the incidence of congenital defects. The study was carried out over a three-and-a-half month period by the State Board of Health.

The Committee sponsored two Round Table discussions at the 1958 annual meeting of the Minnesota State Medical Association, one relating to obstetric hemorrhage, and the other to perinatal mortality.

Contemplated activities for 1958 include (1) a continuation of the maternal mortality studies and (2) the carrying-out of a sampling of hospital obstetric records throughout the State to evaluate completeness of workup and treatment of the patient. This sampling will be done by members of the Committee. Following this study, an attempt will be made to reach conclusions as to what the proper record should embody.

The establishment of an Obstetric Consultation Panel made up of acceptable consultants is contemplated for 1958. Approval of the Council of the Minnesota State Medical Association will be sought, and the Committee will attempt to designate consultants who will serve on a fee basis (payable by the State Board of Health when necessary) so that any physician in the State may have available obstetric consultation within a radius of fifty to seventy-five miles.

JAMES J. SWENDSON, M.D., *Chairman*

WEBER-CHRISTIAN DISEASE

(Continued from Page 650)

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250 mg., 125 mg.

ORAL SUSPENSION (orange flavored)
2 oz. bottle, 125 mg. per tsp. (5 cc.)

PEDIATRIC DROPS (orange flavored)
10 cc., 5 mg. per drop (100 mg. per cc.)
Calibrated dropper

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glucosamine potentiated tetracycline with nystatin

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CAPSULES (black and orange)
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Meetings and Announcements

MEDICAL MEETINGS

State

Conference on Electrical Techniques in Medicine and Biology, eleventh annual session, Nicollet Hotel, Minneapolis, November 19, 20 and 21, 1958.

NATIONAL

Academy of Psychosomatic Medicine fifth annual meeting, Park Sheraton Hotel, New York City, October 9-11, 1958.

American Association of Medical Assistants, Second Annual Meeting, Palmer House, Chicago, Illinois, October 30, November 1 and 2, 1958. All Medical Assistants are cordially invited to attend.

American College of Gastroenterology, 23rd Annual Convention. Jung Hotel, New Orleans, La., October 20, 21, 22, 1958.

American College of Surgeons, 44th annual Clinical Congress, Chicago, Conrad Hilton Hotel, October 6-10, 1958.

American Rhinologic Society, fourth annual meeting, Palmer House, Chicago, Illinois, October 17-18, 1958.

Chicago Medical Society, Postgraduate Courses, 86 E. Randolph Street, Chicago 1, Illinois. Medicine—October 27-31, 1958, and Surgery—November 3-7, 1958.

Fifth Annual Conference of Mental Health Representatives of the State Medical Associations sponsored by the AMA Council on Mental Health, November 21 and 22, 1958, Drake Hotel, Chicago.

Gerontological Society, Inc., Bellevue Stratford Hotel, eleventh annual scientific meeting, Philadelphia, Pennsylvania, November 6, 7, and 8, 1958.

Mississippi Valley Medical Society, 23rd Annual Meeting. Hotel Morrison, Chicago, Illinois, September 24, 25, 26, 1958.

National Society for Crippled Children and Adults, 1958 convention, November 16-20, Statler Hotel, Dallas, Texas.

One-day course in Cardiac Resuscitation, Emory University School of Medicine, Atlanta, Georgia, October 3, 1958. Write Postgraduate Education, Emory University School of Medicine, 69 Butler Street, SE, Atlanta 3, Georgia, for further information.

Orthopedic Surgery and Fracture Postgraduate Course, University of Oklahoma Medical School Auditorium, Monday, September 29, 1958.

Second Oklahoma Colloquy on Advances in Medicine, Arthritis and Related Disorders, University of Oklahoma School of Medicine, Oklahoma City, Oklahoma, November 12, 13, 14 and 15, 1958.

Western Surgical Association, annual meeting, Hotel Kahler, Rochester, November 20, 21 and 22, 1958.

INTERNATIONAL

The international College of Surgeons, fourth Around-the-World Postgraduate Clinic and Lecture Tour. Departure from San Francisco, October 10; return to New York, December 3, 1958.

International College of Surgeons, southeastern regional meeting, Miami Beach, January 4-7, 1959. For information, write to Harold O. Hallstrand, M.D., 7210 Red Road, South Miami, Fla., chairman.

CANCER DETECTION EXAMINATION LIMITED

Following the recommendation of the Cancer Committee of the Minnesota State Medical Association, no new patients will be admitted to the Cancer Detection Center at the University of Minnesota. Letters have been sent to more than 4,000 persons now on the waiting list, informing them of this and asking that they consult their own private physicians for this type of examination.

MINNESOTA ACADEMY OF GENERAL PRACTICE

The Minnesota Academy of General Practice announces the 8th Annual Fall Refresher which will be held Tuesday and Wednesday, October 21 and 22, 1958 at Mayo Civic Auditorium, Rochester, Minnesota.

A full panel of Mayo Clinic personnel will be on hand to deliver ten hours of intensive instruction from 2:00 p.m. through 5:00 p.m. on Tuesday and from 9:00 a.m. through 5:00 p.m. on Wednesday.

Further information may be obtained from James A. Blake, M.D., Executive Secretary, Hopkins, Minnesota.

CONTINUATION COURSES

September 23 to 25, the University of Minnesota will present a continuation course in Pediatrics for Pediatricians at the Center for Continuation Study on the University campus. This course for pediatricians and physicians interested in the field of pediatrics consists of lectures, panels, and round table discussions on "Advances in the Diagnosis and Management of Diseases of Infants and Children."

Visiting participants will include Drs. Daniel C. Darrow, Professor of Pediatrics, University of Kansas School of Medicine, Kansas City; James N. Etteldorf, Professor of Pediatrics, University of Tennessee College of Medicine, Memphis; and Waldo E. Nelson, Professor and Head, Department of Pediatrics, Temple University School of Medicine, Philadelphia. Dr. Darrow will also

(Continued on Page A-46)

They all went to the doctor...

I was too much

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CONTINUATION COURSES

(Continued from Page A-44)

present the Fourth Irvine McQuarrie Lecture at 8:15 p.m., Wednesday, September 24, on "Clinical Observations and Experimental Studies of Body Water." The course will be presented under the direction of Dr. John A. Anderson, Professor and Head, Department of Pediatrics. The remainder of the faculty will include members of the faculty of the University of Minnesota Medical School and the Mayo Foundation.

Other medical continuation courses to be presented at the Center for Continuation Study, University of Minnesota, include:

October 6-8—Obstetrics for Specialists
October 23-25—Dermatology for General Physicians
November 3-8—Pediatric Radiology for Radiologists
November 17-19—Fractures for General Physicians
November 17-22—Neurology and Neurosurgery for General Physicians
November 20-22—Physical Medicine for Specialists

For further information concerning the above courses, write to the Director, Department of Continuation Medical Education, 1342 Mayo Memorial, University of Minnesota, Minneapolis 14.

POSTGRADUATE COURSES ON DISEASES OF THE CHEST

The Council on Postgraduate Medical Education of the American College of Chest Physicians will present the following Postgraduate Courses this fall:

Clinical Cardiopulmonary Physiology—Edgewater Beach Hotel, Chicago, Illinois, October 13-17, 1958.

Diseases of the Chest—Park-Sheraton Hotel, New York City, November 10-14, 1958.

Tuition for each course is $100. Further information may be obtained by writing to the Executive Director, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

According to the Public Health Service, the United States is lowering its guard against diphtheria with the resultant increase in reported cases. The Service urges immunization of all children and in some areas, booster shots for adults.—Christmas Seal *Health News*.

TAKE A NEW LOOK AT FOOD ALLERGENS* TAKE A LOOK AT NEW DIMETANE

DIMETANE Extentabs (12 mg. each, coated) provide antihistamine effects daylong or nightlong for 10-12 hours. Tablets (4 mg. each, scored) or pleasant-tasting Elixir (2 mg./5 cc.) may be prescribed t.i.d. or q.i.d., or as supplementary dosage to Extentabs in acute allergic situations. A. H. ROBINS CO., INC., Richmond 20, Virginia. Ethical Pharmaceuticals of Merit Since 1878.

*Sea food—source of highly potent allergens. Typical are: lobster; tuna; sturgeon roe; fish oil used to prepare leather, chamois, soaps; cuttlefish bone for polishing material and tooth powder; glues made from fish products.

Woman's Auxiliary

FALL WORKSHOP WILL HAVE VACATION AIR

October 9 and 10 will hold much interest for Auxiliary members, when the Fall Workshop will be held at the Biltmore in Minneapolis.

Special note should be made of the fact that this year the workshop will cover portions of a two-day period. Also of special note is the meeting-place—the Biltmore, which offers the advantage of parking space, over-night quarters for those who desire, and eating facilities, plus our meeting place in a private dining room.

A worthwhile program is being planned by the president, Mrs. Reuben Erickson.

Circle these dates NOW!

EDITOR'S NOTE: News items regarding the activities of your county society are essential to well-rounded coverage of all Minnesota State Medical Association Auxiliary activities. Forward news items, newspaper clippings, and other items to Mrs. John Linner, 4619 Drexel, Minneapolis 24, or to the Auxiliary News Editor, Minnesota State Medical Association, 496 Lowry Medical Arts Building, St. Paul 2, Minnesota.

HENNEPIN COUNTY AUXILIARY TEA DATE IS SET

The Woman's Auxiliary to the Hennepin County Medical Society will hold its opening tea on Friday, October 3, from 2 to 4 p.m., at the home of Mrs. Howard Frykman, 6212 South Knoll Drive, Minneapolis. New members and officers will be honored and members of the Student American Medical Association will be guests.

Every journey to a forbidden end begins with the first step; and the danger of such a step by the federal government in the direction of taking over the powers of the states is that the end of the journey may find the states so despoiled of their powers, or—what may amount to the same thing—so relieved of the responsibilities which possession of the powers necessarily enjoins, as to reduce them to little more than geographical subdivisions of the national domain.—JUSTICE GEORGE SUTHERLAND.

In a recent 140-patient study[1] DIMETANE gave "more relief or was superior to other antihistamines," in 63, or 45% of a group manifesting a variety of allergic conditions. Gave good to excellent results in 87%. Was well tolerated in 92%. Only 11 patients (8%) experienced any side reactions and 5 of these could not tolerate any antihistamines.

Robins

1. Thomas, J. W.: Ann. Allergy 16:128, 1958

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A-47

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1. Hodges, F. T.: *GP* 14:86, Nov., 1956.

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In Memoriam

IRVING JEFFERY GLASSBERG

Dr. Irving J. Glassberg, clinical instructor at the University of Minnesota Medical School, died July 28, 1958. He was fifty-one years old. His specialty was urology.

A native of Minneapolis, he returned to the city two years ago after practicing for more than twenty years in New Orleans, Louisiana. He attended the University of Pennsylvania and received his M.D. degree from the University of Minnesota in 1935.

In Louisiana, he was assistant clinical professor at the University of Louisiana Medical School and served as head of the urology department at the Touro Infirmary in New Orleans.

Dr. Glassberg was a member of Hennepin County Medical Society, Minnesota State Medical Association and the American Medical Association. He was a member of the Board of Temple Israel. Other memberships held by Dr. Glassberg include the American College of Surgeons, American Board of Urology and the American Urological Association. His fraternities were Zeta Beta Tau and Phi Delta Epsilon.

He is survived by his wife, Raleigh; two sons, John

(Continued on Page A-50)

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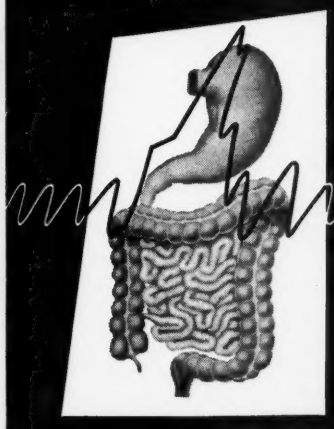

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SEARLE

IRVING JEFFERY GLASSBERG

(Continued from Page A-48)

and Jeffery, and a daughter, Raleigh, Minneapolis; his mother, Annette Glassberg, Bronxville, New York; and a sister, Mrs. Lester Isaac, also of Bronxville.

RICHARD B. GIRVIN

Dr. Richard B. Girvin, formerly of Minneapolis, died August 7, 1958, in St. Louis, Missouri. He was seventy-four years of age.

Dr. Girvin, who was born in Mankato, was a graduate of Hamline University, St. Paul, and University of Minnesota Medical School. He practiced medicine in Minneapolis for over thirty years and was on the staffs of St. Barnabas and St. Andrew's Hospitals.

He was a member of the American Medical Association, a life member of the Minnesota State Medical Association, Hennepin County Medical Society, Minnesota Medical Society of Military Surgeons and Aero Medical Association.

In World War I, Dr. Girvin was a captain in the Army Medical Corps and served in France and at Walter Reed Hospital, Washington, D. C.

Surving are a son, Richard W., St. Louis; a daughter, Mrs. Lloyd Hackley, Cleveland, Ohio; and two grandchildren.

ANNAH HURD

Dr. Annah Hurd, a practicing physician in Minneapolis for more than fifty years, died Thursday, July 24, 1958. She was eighty-six years old. Her retirement was announced in 1956.

Dr. Hurd graduated from the University of Minnesota's School of Pharmacy in 1896 and the School of Medicine in 1900. She later did graduate work at Northwestern University.

She was a member of the Hennepin County Medical Society and a life member of the Minnesota State Medical Association.

NURSE SHORTAGE

The Department of Labor estimates that this country's shortage of nurses has reached 70,000. The number available was estimated at about 430,000.

Simultaneously, the American Nurses' Association issued a statement expressing deep concern over the rapid expansion of hospitals in the face of the critical shortage of nurses and other health personnel.

The Labor Department's estimate is included in a twenty-seven-page pamphlet, "Nurses and Other Hospital Personnel," giving suggestions to communities on how to increase the nurse supply. Among these were recruitment programs, salary rises, encouragement of former nurses to return to work and encouragement of older women to become practical nurses.—*New York Times.*

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Communications

This Section is for you to voice your convictions, comments, and queries on all subjects political, economic, historic, humorous, scientific or otherwise, to many physicians. Writings not sufficiently formal and too brief for an editorial or a scientific manuscript are requested. Clinical and research observations, no matter how brief, similar to those in *The Lancet* (London), are particularly encouraged.

SILO-FILLER'S DISEASE INVESTIGATIONS

To the Editor:

The co-operation of physicians is being sought by the University of Minnesota in its study of silo-filler's disease.†

The School of Public Health and the Departments of Pathology, Radiology and Medicine of the Medical School, with the assistance of a grant from the National Institutes of Health, are engaged in a comprehensive study of human poisoning by silage gas. In addition to studies on pathogenesis and the biochemical aspects of the ensiling process, an important phase of the study involves epidemiologic inquiries on a random sample of farmers potentially exposed to silage gas and among suspect cases brought to our attention from a number of sources including practicing physicians.

The objective of this phase of the study encompasses the determination of prevalence of this disease entity which undoubtedly manifests itself in a spectrum of clinical illness ranging from early death due to massive pulmonary edema, through delayed death from bronchiolitis fibrosa obliterans, survival with chronic pulmonary insufficiency due to fibrosis and/or emphysema, to a simple chronic bronchitis or even complete recovery without sequelae. Furthermore, the role of silage gas (NO_n) poisoning in the production of chronic pulmonary disease is being sought and more-or-less quantitative correlations between clinical disease and degree of exposure to such gas are being explored.

Since the true incidence of such poisoning and the prevalence of sequelae is not known, a tremendous contribution to research in these several aspects of this study can be made by practicing physicians of the state.

Your co-operation is thus being urgently requested in notifying us of any probable or suspect case of exposure to silage gas or illness even remotely associated with filling of silos or with entry into silos for the two-week period after filling or refilling.

Upon receipt of such reports, a member of our investigating team will contact each reporting physician for clinical information and permission to interview the case relative to the circumstances of exposure.

LEONARD M. SCHUMAN, M.D.
Professor of Epidemiology and Director of Silo-Filler's Disease Studies

1158 Mayo Building
University of Minnesota
Minneapolis 14, Minnesota

†University of Minnesota Medical Bulletin 27, 234, May 1, 1956, and the J.A.M.A., 162:153, Sept. 15, 1956.

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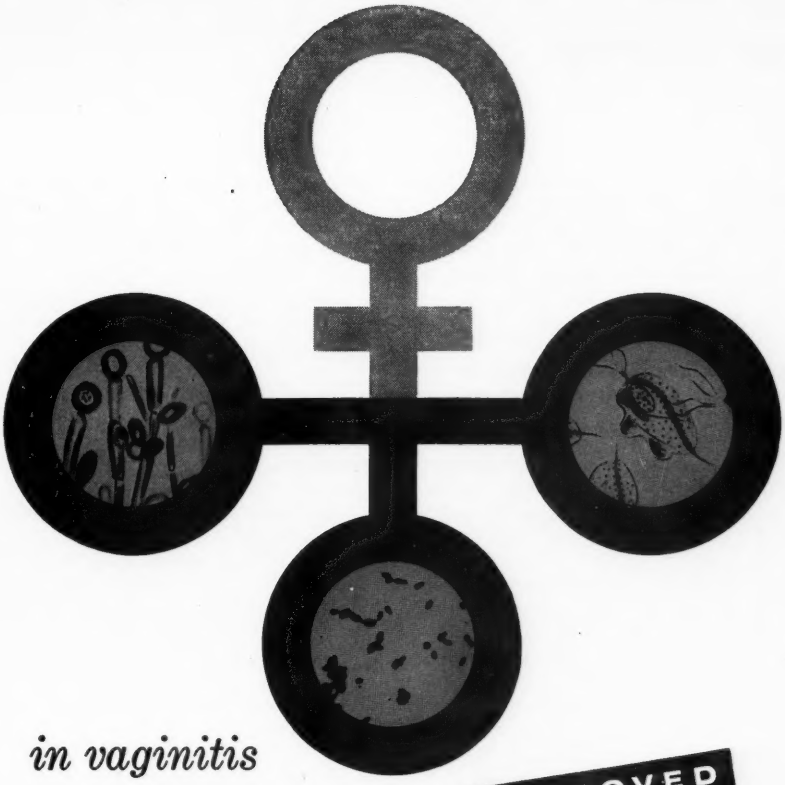

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General Interest

Dr. John R. McDonald, head of a section of surgical pathology in the Mayo Clinic, and professor of pathology in the Mayo Foundation, Graduate School, University of Minnesota, left Rochester on July 1 to become director of pathology at the Harper Hospital in Detroit, Michigan. Dr. McDonald has been a member of the staff of the Mayo Clinic since 1937.

* * *

Dr. A. G. Athens, Duluth, recently attended the International Congress of Ophthalmology in Brussels, Belgium.

* * *

Dr. William E. Eisenstadt, Minneapolis, recently spoke before the Blue Earth Valley Medical Society at Fairmont on the subject, "The Management of Bronchial Asthma, including Status Asthmaticus."

* * *

Dr. Charles G. Moertel has been appointed a consultant in medicine in the Mayo Clinic, Rochester.

* * *

Dr. Leland R. Christenson opened offices for general practice in Maple Plain, Monday, July 14. Dr. Christenson is a native Minnesotan from Marshall. He took his pre-medical training at St. Olaf College in Northfield, receiving his B.A. degree in 1953. He attended medical school at the University of Minnesota, from which he received his B.S. and M.D. degrees in 1957. Dr. Christenson was the second recipient of the Minnesota Rural Medical Student Scholarship. This scholarship is given by the Minnesota State Medical Association to one student each who intends to enter general practice in a town of less than 5,000 population in Minnesota. Dr. Christenson took his internship at Bethesda Hospital, St. Paul.

* * *

Drs. F. G. Elias and **H. E. Bakkila,** Duluth, attended the American Medical Association meeting in San Francisco on June 23-27.

* * *

Dr. Asa Graham, formerly of St. Paul, has joined the medical staff of the Faribault Medical Center, 924 N.E. First, and has begun the general practice of medicine and survery.

* * *

Dr. James H. Kelly, a native of De Graff, has opened offices at 204 Granite Exchange Building, St. Cloud, for the practice of internal medicine.

* * *

Dr. Ben Owens, Hibbing, won the Pfizer award at the Physicians' Golf Tournament in Virginia recently.

* * *

Dr. Harvey E. Sisk, St. Cloud physician, has been elected to the board of directors of the Minnesota Heart Association.

* * *

Dr. W. O. B. Nelson began the practice of medicine in Sanborn recently. Dr. Nelson is a graduate of Hamline University and the University of Minnesota's School of Medicine. He practiced internal medicine at Fergus Falls for twenty years, and the past year has been in general practice at Bisbee, Arizona.

* * *

Dr. Ralph E. Smith, Minneapolis, has been appointed a consultant in medicine in the Mayo Clinic, Rochester. Since 1954, Dr. Smith had been assistant professor of medicine in the University of Minnesota Medical School.

* * *

Effective August 1, **Dr. D. Robert Nelimark** became associated with **Dr. J. A. Callan** and **Dr. W. S. Neff** in the department of internal medicine at the Lenont-Peterson Clinic in Virginia.

* * *

Dr. Henry Korda, Pelican Rapids, was recently appointed to the Board of the Fergus Falls Mental Health Clinic, according to Roland F. Winterfeldt, Executive Secretary of the Otter Tail County Welfare Board.

* * *

Dr. Robert K. Sommer, a graduate of Indiana University, has joined the staff of the Elk River Clinic.

* * *

Dr. Cleon R. Holland has been appointed to the staff of the Mayo Clinic in Rochester. He will be a consulting physician in the emergency and admitting room of St. Mary's Hospital in Rochester. Dr. Holland had been a fellow in surgery of the Mayo Foundation since January 1, 1954.

"IT ALL STARTED WHEN HE WAS PUTTING TOGETHER ONE OF THOSE 'ANY CHILD CAN ASSEMBLE IT' TOYS!"

Dr. Russell O. Sather, Crookston, has been elected to the board of directors of the Minnesota Heart Association for 1958-59. He was among the new members named at the Association's annual meeting in St. Paul. Research grants of $200,010 were distributed to fifty-five Minnesota heart scientists at the meeting.

* * *

Dr. Milton Abrahamson, with offices at 502 Medical Arts Bldg., and Westwood Medical Center, 2301 Louisiana Ave., St. Louis Park, announces the association of **Dr. Robert K. Nolan** in the practice of obstetrics, gynecology and infertility.

* * *

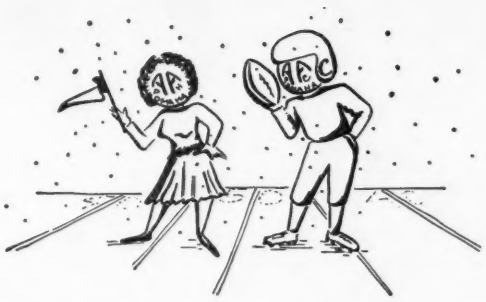
Dr. W. G. Tomhave, Hibbing, has taken a leave of absence from the Mesaba Clinic to take a residency at the Veterans Administration Research Hospital in Chicago.

* * *

Five Wayzata physicians will locate in the new Wayzata Medical Building, currently under construction. They are **Drs. Robert Semsch, Deane A. Petersen, E. J. Huenekins, F. J. McCaffrey** and **George O. Hilgermann.** The new structure is located on Highway 101, just north of Highway 12.

* * *

Dr. Harry A. Wilmer, a consultant in psychiatry in the Mayo Clinic since July 1, 1957, has resigned from the staff of that institution as of July 1, 1958, and is now in Palo Alto, California, where he will carry on the private practice of psychiatry.



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Dr. J. A. Winter, Duluth, attended the regional meeting of the American College of Surgeons at Stockholm, Sweden, on July 2-7.

* * *

Dr. Roger R. Miesfeld, formerly of Columbus, Ohio, has recently joined with **Dr. R. T. Seashore** and **Dr. K. W. Teich,** of Duluth, in the practice of obstetrics and gynecology. Dr. Miesfeld, a native of Wisconsin, is a medical school graduate of George Washington University of Washington, D. C., and has just completed a four-year residency at Ohio State University in Obstetrics and Gynecology, receiving his master's degree in June.

* * *

Dr. and Mrs. Virgil J. Schwartz, Minneapolis, left on August 16 for an extended European tour, in the course of which Dr. Schwartz attended the eighteenth annual meeting of the International Academy of Ophthalmology in Brussels on September 8. They will visit Spain, France, Denmark, Switzerland, England and Scotland, as well as Belgium and Austria, before returning to Minneapolis.

* * *

Dr. Adelaide M. Johnson, Rochester, clinical professor of psychiatry in the University of Minnesota Medical School, recently spoke on "Special Features of Child Psychiatry" on the program of the Institute on Psychiatry and Religion. These annual institutes are devoted to a study of problems common to psychiatry and the clergy. This year's institute was held at the College of St. Catherine in St. Paul.

* * *

Eleven Minnesota scientists have been named recipients of national heart research grants-in-aid totaling $82,249.20 from the American Heart Association and its affiliates. The new awards will boost Heart Fund-sponsored research spending to a record $348,759.20 in Minnesota during the current fiscal year, according to Dr. Karl W. Anderson, president of the Minnesota Heart Association. The awards were among 226 totaling $1,540,457, announced by the AHA. Scientists working in thirty-six states and one foreign country (Lebanon) are sharing the grants, two-thirds of which are in the field of basic research. With the new awards the total channeled into heart research by Heart Fund agencies now tops $31.5 million in the past ten years. Named in Minnesota were **Dr. W. O. Lundberg, Dr. Richard A. DeWall, Dr. Robert A. Good, Dr. Ralph T. Holman, Dr. Ancel Keys, Dr. Laurence O. Pilgeram, Dr. Edward Ronwin, Dr. Ernst Simonson, Dr. Henry L. Taylor, Dr. Louis Tobian,** and **Dr. Richard W. Vorhees Korff.**

* * *

Dr. Leland G. Reichelt, Roseau, has associated with the Davis Clinic in Wadena. He replaces **Dr. John N. Heinz** who has been called into the army medical corps.

* * *

The following officers were elected at a recent meeting of the Ada Hospital staff: **Dr. Theo. Loken,** Ada, president or chief of staff; **Dr. Byron Kinkade,** Ada, vice president; **Dr. Clifford Stadum,** Twin Valley, secretary. Dr. Loken appointed **Dr. E. Erickson,** Halstad,

as chief of medical records committee to be assisted by Dr. Kinkade. Appointed by Dr. Loken as chief of tissues committee is Dr. Stadum, to be assisted by Dr. Loken. Drs. Kinkade, Stadum and Erickson will be members of the Executive, Joint Conference and Credentials Committee headed by the chief of staff.

* * *

Dr. Arthur J. Rushay recently joined **Drs. A. E. Muller** and **Charles J. Beck** in their medical practice in North Saint Paul.

* * *

Dr. Roy H. Good began practicing medicine in Northfield on September 1. He has been practicing at Glenwood for the past five years.

* * *

Dr. John S. Lundy, of the Mayo Clinic, Rochester, has been appointed a consultant-lecturer in anesthesiology to the Surgeon General of the U. S. Navy, it has been announced by Rear Admiral E. C. Kenney, of Washington, D. C., assistant chief for personnel and professional operations of the Bureau of Medicine and Surgery of the Navy. Dr. Lundy founded the Section of Anesthesiology at the Mayo Clinic in 1924. He carried on a training program for members of the armed forces at the Mayo Clinic during World War II, and has written a book on clinical anesthesiology and made many other contributions to literature in this field.

MINNESOTA STATE BOARD OF MEDICAL EXAMINERS

MINNEAPOLIS WOMAN SENTENCED IN ABORTION CASE

On August 6, 1958, Elvira Bernice Nelson appeared before the Hon. Levi M. Hall, Judge of the District Court of Hennepin County, and entered a plea of guilty to an information which charged her with the crime of abortion. Judge Hall then sentenced Mrs. Nelson to be imprisoned in the State Reformatory for Women at Shakopee for a term not to exceed one year. Immediately thereafter, Judge Hall stayed the execution of the sentence and placed the defendant on probation for one year. Mrs. Nelson, a widow, who was born at Winger, Minnesota, on September 15, 1917, resided at 2629 36th Avenue South, Minneapolis, at the time of her arrest.

The case came to the attention of the authorities when the defendant became ill following a criminal abortion and was hospitalized at Minneapolis General Hospital. Mrs. Nelson did not co-operate with the authorities in naming the abortionist until after a representative of the Minnesota State Board of Medical Examiners had signed a complaint charging her with a crime as stated above. She later gave a full statement which disclosed that she had been aborted by a Minneapolis man on June 14, 1958, after being informed that the fee for the operation would be $500. The Hennepin County Attorney's office then issued an abortion complaint against the man named by Mrs. Nelson, and he was awaiting trial when the defendant Nelson was sentenced.

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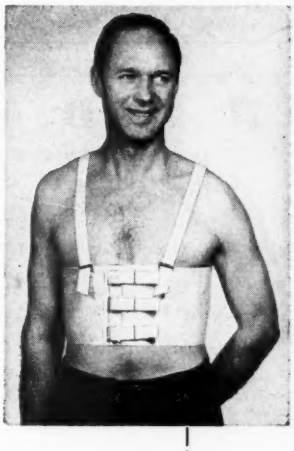

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Book Reviews

Books listed here become the property of the Ramsey, Hennepin and St. Louis County Medical Libraries when reviewed. Members, however, are urged to write reviews of any or every recent book which may be of interest to physicians.

BOOKS RECEIVED

A DOCTOR SPEAKS HIS MIND. Roger I. Lee, M.D. Formerly on Board of Trustees of American Medical Association; formerly president of the American College of Physicians, professor of hygiene at Harvard, member of Harvard Corporation and a founder of the Harvard School of Public Health. 120 pages. Price $3.00, cloth. Boston: Little, Brown & Co., 1958.

ELECTROCARDIOGRAPHY. Michael Bernreiter, M.D., F.A.C.P. Assistant Clinical Professor of Medicine, University of Kansas Medical School; Chief of Electrocardiography, St. Mary's Hospital, Kansas City, Missouri; Fellow of the American College of Cardiology and Fellow of the American College of Chest Physicians. 134 pages. Illus. Price $5.00, cloth. Philadelphia: J. B. Lippincott Company, 1958.

THERAPEUTIC USES OF ADHESIVE TAPE. 130 pages. Illus. Cloth bound. New Brunswick, N. J.: Johnson & Johnson, Second Edition, 1958.

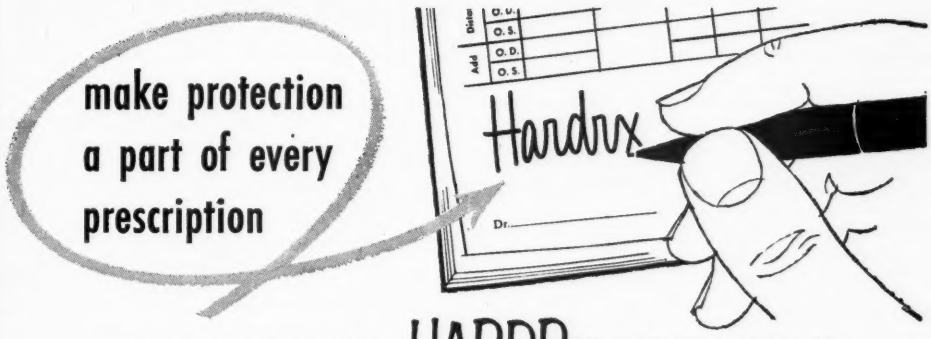
CLINICAL OBSTETRICS AND GYNECOLOGY. Vol. 1, No. 2 of quarterly series. Toxemias of Pregnancy, Edited by Louis M. Hellman, M.D., and Fibromyomas of the Uterus, Edited by Robert A. Kimbrough, M.D. Illus. Price, $18.00 per year, cloth bound. New York: Paul B. Hoeber, Inc., 1958.

IDEALS IN MEDICINE. A Christian Approach to Medical Practice. Edited by Vincent Edmunds, M.D., M.R.C.P., and C. Gordon Scorer, M.B.E., M.D., F.R.C.S. 192 pages. Price $3.00, cloth. Chicago: The Christian Medical Society, 1958.

PATHOLOGY FOR THE PHYSICIAN—William Boyd, Professor Emeritus of Pathology, University of Toronto; Visiting Professor of Pathology, University of Alabama; formerly Professor of Pathology, University of Manitoba and the University of British Columbia. Sixth Edition. 489 illustrations and 12 plates in color. Cloth, $17.50. Philadelphia: Lea & Febiger, 1958.

This book is written in Dr. Boyd's usual interesting and almost story-like manner. Throughout its pages he attempts to correlate clinical and pathologic data. Thus, it is not as complete as a standard text in medicine or as complete as a standard text in pathology. The chapters are arranged to cover the individual organs and their most prominent diseases. The busy practitioner will find this volume useful for a review of the high points of the pathology and the correlation of the clinical manifestations of many major diseases.

JOHN P. KNOEDLER, M.D.



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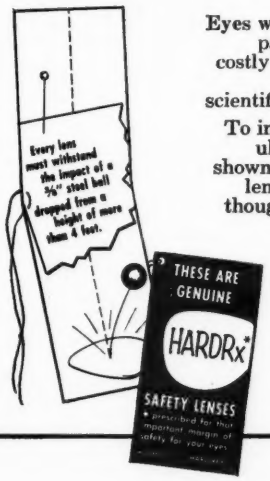

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BOOKLET FOR FAMILIES OF STROKE PATIENTS

A new booklet, entitled "Strokes, a Guide for the Family," has been published by the American Heart Association and its affiliates. As the title indicates, it was prepared primarily for those who live with or care for the stroke patient. Copies of this booklet are available from local Heart Associations and may be requested by physicians to give to the families of such patients. Copies may also be obtained by nurses, physical therapists, speed therapists, and others concerned with the rehabilitation problems of stroke sufferers.

The booklet emphasizes the importance of early rehabilitation and of close co-operation between the physician and members of the family in helping stroke patients regain many of their abilities. It gives specific suggestions for self-help devices that can be used at home and also lists a number of sources through which additional help may be sought during the rehabilitation process. Also included are recommendations for the families of patients requiring treatment over a long period of time and a discussion of the special problems of the patient with aphasia.

Classified Advertising

Replies to advertisements with key numbers should be mailed in care of MINNESOTA MEDICINE, *2642 University Avenue, Saint Paul 14, Minnesota.*

WANTED GENERAL PRACTITIONER—Twin Cities suburban area. New clinic building. Immediate opening. Address E-613, care MINNESOTA MEDICINE.

WANTED GENERAL PRACTITIONER—Prosperous farming community, 15-mile area including seven communities, now without a physician, two good hospitals within 25 miles over excellent roads. Write Reverend Leonard Gaida, Holdingford, Minnesota.

GENERAL PRACTITIONER WANTED — Western Minnesota group desires to add G.P. Well-established group in own building with excellent future opportunities. Address E-646, care MINNESOTA MEDICINE.

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MEDICAL CLINIC—Drug Dispensary, no competition, North Dakota. Grossing $75,000. New brick-frame building; air conditioned; A-1 equipped. Beautiful home optional. Reasonable. REO, 6th West 10th, Kansas City, Missouri.

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MEDICAL AND SURGICAL GROUP would like to form association with young doctor interested in one, two, or three-year appointment as assistant in surgery, and to assist in handling emergency and industrial cases. Address E-642, care MINNESOTA MEDICINE.

WANTED—General Practitioner with ENT experience in small western Minnesota city to associate with small group. To become full partner in three years. Address E-648, care MINNESOTA MEDICINE.

WANTED—Internist, General Surgeon and General Practitioner with special interest in Obstetrics and/or Pediatrics. Salary on contract basis for one to two years and then eligibility for partnership in a five-man group. Complete clinical facilities with good hospital staff association. Address E-653, care MINNESOTA MEDICINE.

OPENING FOR GENERAL PRACTITIONER—Clinic at St. Croix Falls, Wisconsin, needs young general practitioner for either locum tenens or permanent situation. Please call collect St. Croix Falls No. 236, or write K. R. Taylor, St. Croix Falls Clinic.

GOVERNMENT SURPLUS—MEDICAL SUPPLIES—Brand new, first quality surgical instruments and hospital supplies. Write for our medical surplus catalog—lists more than 7500 items for the surgeon, specialist, general practitioner. Catalog contains separate listing in General Surgery—Scissors and Hemostets; Syringes and Needles—Dressings; EENT—Rhinoplastic; Bronchoscopy; Gynecology—Obstetrics; Proctology—Urology; Orthopedics—Neurosurgery; Sutures; Laboratory Supplies—Office Equipment. All merchandise sent subject to your approval. Prompt shipments—we ship anywhere. Arista Surgical Company, 67 Lexington Avenue, New York 10, New York.

FOR SALE—Completely equipped office, southern Minnesota city, 9,000 population. $20,000 gross annually. Address E-621, care MINNESOTA MEDICINE.

FOR RENT—Unopposed General Practice, completely equipped. One-year trial basis with option to buy possible. Available July 1, 1959. Owner specializing. Address E-652, Care MINNESOTA MEDICINE.

FOR RENT—One-story medical building, 900 square feet, air-conditioned. Waiting room, laboratory, seven examining rooms, office. Very efficient unit. Morningside-Edina area. Telephone WAlnut 7-9557, Minneapolis.

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